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No. 1

Original Communications

RADIUM THERAPY OF CARCINOMA UTERI*

TEN YEARS OF CLINICAL EXPERIENCE AND RESULTS AT THE WOMAN'S HOSPITAL

BY GEORGE GRAY WARD, M.D., F.A.C.S., NEW YORK, N. Y.

I HAVE no apology to offer for having the temerity to bring to your attention a subject that has been so ably presented to you only a little more than a year ago by Dr. Polak, because, as he then pointed out, as yet the therapy of cancer of the uterus is by no means accepted and standardized as are most of our gynecologic problems, and because the literature is full of conflicting opinions as to the results obtained, and as to what is the most efficient technic. Therefore, in the hope that our few drops of clinical experience in the radium therapy of carcinoma uteri during the past ten years at the Woman's Hospital may act as a reagent to help clarify the hazy mixture of the various clinical reports, I beg leave to give you a survey of our observations and viewpoint as a small contribution toward bringing about the stabilization of the therapy which I am sure we all ardently desire.

It has been estimated that there are probably 300,000 suffering from cancer in the United States at the present time with a death rate of 89.4 per 100,000, and according to Hoffman 40 per cent of the women dying from cancer in 1923 had the disease in the genital organs or breasts. As you know scarcely any age is exempt; Dr. Bonner's case of carcinoma of the cervix in a girl of thirteen years has been recently reported. Our earliest age is twenty-six years. Twenty years ago, I published a report of a case of primary carcinoma of the vagina in a girl nineteen years of age. It may be of interest to note that this was my first experience with radium therapy. Through the

*Read by invitation at a meeting of the Brooklyn Gynecological Society, April 13, 1928.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

courtesy of Dr. Morton, son of the discoverer of ether anesthesia, we applied four tubes in tandem each containing 10 mg. of radium salt for one hour on three alternate days, it is needless to say, without any benefit.

In my opinion the outstanding contribution to the recent literature on the subject is Heyman's masterly study of the published operative and radiologic statistics of the leading clinics and authorities in Europe and this country, which he presented before the Scandinavian Surgical Society at Gothenburg in June, 1927, and it will well repay us to spend a few moments in a brief survey of his paper.

In this exhaustive analysis Heyman compares the radical operative results with irradiation for carcinoma of the cervix. He calls attention to the difficulties of giving a correct comparative evaluation of both methods due to the fact that while the radical operation has a background of more than twenty-five years with a completed technic whose further advance is not to be expected, radiologic therapy of cervical cancer has a scant fifteen years of experience with the war stopping much investigation, and with the technic still new and under development and by no means standardized. The prime obstacle to comparing the results of both methods is the marked difference in the initial material—that is the degree of progress of the disease when the case is first seen, the initial material coming to the radiologic clinics being mostly advanced (Classes III and IV) inoperable cases, while the reverse is true in the surgical clinics. The technic of the radical operation naturally developed from the most favorable cases and progressed to the more advanced ones. The reverse is the case with radium.

Heyman shows this in a table of operability percentages of different clinics, and reminds us that the hopeless cases were the only ones referred to the radiologist by the surgeon until recently, and points out that this unquestionable difference in the character of the initial material is an overlooked source of error working to the disadvantage of radium statistics. Therefore, it is evident that to obtain a proper evaluation we must compare the results of operation and irradiation in *operable cases only*.

This can only be done tentatively at the present time, because there are too few cases of irradiation available from all the clinics to compare with the great number of operable cases that have been operated radically and observed for five or more years.

In his comparative study of published statistics, Heyman has reduced the figures of all the clinics to one uniform standard. He has left out all doubtful statistics and does not deduct intercurrent deaths or nontraced cases, and quotes only the accepted five-year cure.

The *operative statistics* from twenty clinics reduced to the above standard show a total of 5024 cases of all classes of whom 905 had a five-year cure, or approximately 18 per cent. The results in the early cases (Classes I and II) show 3659 cases with 1303 cured, or 35.6 per cent. But the primary mortality from the operation was 17.2 per cent. The operability of the total cases seen was more than 43 per cent.

The *radiological statistics* from seventeen clinics reduced to the same standard show a total of 3512 cases of all classes with 571 cured for five years, or 16.3 per cent.

The results in the operable and borderline cases (Classes I and II) show 960 cases with 335 five year cures, or 34.9 per cent.

The primary mortality from irradiation would be probably less than 2 per cent (Radium-hemet was 1.59 per cent). The operability of the total cases seen was less than 30 per cent.

To recapitulate, Heyman's combined summary of *all* clinics shows:
Cures for total cases—Operative treatment = approximately 18 per cent; Radiologic treatment = 16.3 per cent.

Cures for operable and borderline cases—Operative treatment = 35.6 per cent; Radiologic treatment = 34.9 per cent.

Primary Mortality—Operative treatment = 17.2 per cent; Radiologic treatment = approximately 2 per cent.

While these figures apparently approach each other very closely, it must be evident that it is not fair to consider them as similar when we take into account the great difference in the character of the initial material as shown by a 43 per cent operability in the operative statistics as compared to less than 30 per cent in the radiologic figures.

The above general averages are interesting when compared with the results obtained at the Radium-hemet at Stockholm by Forsell and Heyman. From 1914 to 1921, inclusive, they treated 502 cases with an operability percentage of 29.1 per cent; 22.4 per cent were free from symptoms after five years. There were 145 operable and borderline cases with a five-year cure of 44.4 per cent. Their primary mortality from irradiation was 1.59 per cent.

These results contrasted with the general average of the operative treatment are certainly to the advantage of irradiation therapy, especially when we consider the character of the initial material from which these figures are compiled.

In 1925, we reported our results at the Woman's Hospital of two five-year series of radium therapy for carcinoma of the cervix before the American Medical Association. Our percentage of cures of all cases (76) was 23.6 per cent and for the early and borderline (operable) cases was 52.9 per cent based on cases traced, or 22.4 per cent, and 50 per cent when including the nontraced cases, to accord with Heyman's uniform standard, with a mortality of 1.6 per cent. Since that date we have completed two more five-year series and are now able to report on all cases treated in 1919, 1920, 1921, and 1922 and the first five months of 1923. Our records and follow-up end-result cards have been audited by Merwin and Davis, professional statisticians, and the figures I present to you have been compiled by them and certified as correct. This report includes only cases of primary carcinoma of the cervix treated by us by irradiation alone throughout the course of the disease.

We have treated a total of 154 cases of carcinoma of the cervix for five years or longer with radium alone during the nearly ten-year period that we have had radium at our disposal. One hundred thirty-four were primary cases treated with radium alone, of whom we have

traced all but eight with 23.1 per cent of five-year cures. There were 32 operable cases (early or borderline), Classes I and II, of whom we have traced all but 2 with 53.1 per cent of five-year cures.

We have 15, or 15.5 per cent, living six years; 11, or 15.5 per cent, living seven years; and 4, or 9.5 per cent, living eight years. These results compare with Heyman's combined statistics and with the Radium-hemet as follows:

<i>Total Cases Treated</i>			
<i>All Clinics</i>	}	Operative treatment	18 per cent
		Radiologic treatment	16.3 per cent
		Radium-hemet	22.4 per cent
		Woman's Hospital Clinic	23.1 per cent
<i>Operable Cases</i> (early and borderline)			
<i>All Clinics</i>	}	Operative treatment	35.6 per cent
		Radiologic treatment	34.9 per cent
		Radium-hemet	44.4 per cent
		Woman's Hospital Clinic	53.1 per cent

Although our total series is small as compared to the Radium-hemet, still it is encouraging to know that our last two five-year series maintain the percentages achieved in our previous report. It must be borne in mind that the percentages given for the borderline cases must always be of uncertain value, as "borderline" means confusion because it must depend entirely upon the personal equation of the surgeon. We are inclined to agree with Jeff Miller, that it is a useless classification for practical purposes and that we should simplify our statistics by having only two types—early and advanced. Likewise there must be uncertainty as to the term "operability," because one surgeon will consider operable and will operate on cases with definite involvement of the parametrial tissues, as for instance Victor Bonney, while many of us, who are conservative, will not consider a case operable unless the uterus is mobile and without infiltration beyond the cervix. Consequently, the figures given for "operable" cases will always be of unstable value for comparison also.

The lack of standardization of statistical reports is what complicates the problem of making fair comparisons. A cursory glance at the various reports published in the literature will show what a great variability exists in presenting the subject. Two, three and four-year results only add to the confusion and should be abandoned. Only five-year observations should be considered.

In reporting radium therapy statistics I believe that the five essentials should be:

1. A uniform classification as to the extent of the disease.
2. Five-year results of total treated cases, early and advanced.

3. Five-year results of the early cases—that is definitely confined to the cervix—operable cases.

4. The operability rate.

5. The primary mortality.

If all clinics would simplify their reports so as to follow these requirements, our task of giving proper values to the various technics employed would be greatly facilitated.

TECHNIC AT THE WOMAN'S HOSPITAL CLINIC

We have not a large amount of radium at our disposal at the Woman's Hospital; our armamentarium consists of some 280 milligrams of the salt in tubes and needles, and our average initial dosage has been from 2400 to 4200 milligram hours. It is of interest to note that the Radium-hemet at Stockholm also uses the salt in similar dosage, and does not use the emanation with massive amounts. Our results force us to believe that the employment of massive doses cannot show any better results than the intelligent application and reapplication of smaller doses.

We start with the principle that every case of cancer of the cervix is a study in itself, and that the *frequent personal observation* by the surgeon directing the treatment is absolutely essential to obtain results, and this personal contact must continue throughout the period of cure. As we cannot say when any case is permanently cured, this means the patient should be under observation at regular intervals throughout her life, if she would be safe, as we believe we have obtained our results by this constant watching enabling us to discover a recrudescence of the disease in its early stages long before the patient would be aware of symptoms. Thus we have the opportunity of putting out the fire while it is yet a small blaze by prompt reradiation, instead of having to try and extinguish a serious conflagration which would be present when the patient had developed symptoms. If there is an opportunity to plant a radium needle in a suspicious area at the onset of a recurrence, the problem is much simpler, as the chances of smothering the fire in its incipency are greater. We, therefore, believe in repeated reradiations as often as indicated. Nearly 50 per cent of our cases have had more than one application, and many of our successful cases have had three or more irradiations. It is upon this personal frequent follow-up of our cases that we have based our treatment, and attribute to it whatever success we have had.

As we are familiar with what the post radiation picture should be at the end of each month, we think we can tell from the general appearance of the growth whether the several stages of hyperemia, local sloughing, separation of slough, and healing process with final cicatrization and marked contraction, which represent the phenomena of irradiation of the cervix by radium, are progressing satisfactorily.

This process, as we have observed it at our clinic, has been graphically shown in a paper published by Farrar. Our technic of application is simple and has been described in a previous report. We employ brass and rubber screening of the radium tube and distance screening with vaginal gauze for the protection of the bladder and rectum. We believe anchoring of the radium tube by suture is an important detail. We prefer the short needles to the long model for implantation in the periphery of the growth, and we believe the needles should not be closer to each other than two centimeters. Usually four needles are sufficient unless the growth is very large. We have found a self-retaining catheter inserted in the bladder during the time of the radium application is most satisfactory to all concerned.

Many of these patients are suffering from toxic absorption and are cachectic and anemic. During the sloughing stage of the radiation process there is necessarily an increased absorption of these toxins with resulting septic fever and an increase of the debilitated state. We have found that blood transfusion is an important adjunct to the irradiation in enabling these patients to combat this sepsis more successfully. Wherever possible we give these cases 500 c.c. of blood before their discharge from the hospital.

An important detail is to get the patient up early to favor drainage and to give careful instructions as to repeated daily douches of potassium permanganate solution to favor separation of the slough, to deodorize it, and to stimulate tissue growth.

Our results have been obtained without the employment of high voltage x-ray therapy as an adjunct as we have not the apparatus, and our employment of a moderate voltage as a post radiation treatment in some of our cases seemed harmful, and gave us no more satisfactory results than when we used radium alone. So for the present we do not use x-ray therapy in conjunction with radium as a routine. We believe, however, that high voltage attack on the lymphatic glands to produce a lymphatic block as an adjunct to radium therapy is theoretically correct, and if it can be done without associated injury to the adjacent viscera it would be ideal.

Observations during ten years' experience with the personal follow-up of our cancer cases has enabled us to form certain definite opinions as to what we may expect from radium therapy, and I have selected the following cases as illustrative examples of our experience from a special file labeled "remarkable cases."

a. *Hopeless Cases.*—We have learned to reserve judgment on the outcome of the apparently hopeless cases.

For instance, Mrs. B. (21680) came to us with extensive carcinoma of the cervix, Class III, in June, 1919. Her previous weight was 219 pounds. She had three applications of radium, the last in March, 1920, developed vesicovaginal and rectovaginal

fistulae, and was admitted to the House of Calvary in June, 1920, weighing 100 pounds as having but a short time to live. She returned to us in July, 1921 with the rectovaginal fistula healed, feeling fine and weighing 233 pounds. She has a vesicovaginal fistula, but fortunately it is situated high up, so that by frequent emptying of the bladder she is fairly comfortable and is strong and able to do her daily work. She is well today after 8 years and 9 months.

Another example is Mrs. D. (32729). Carcinoma of cervix, Class III; first treatment in August, 1923, second treatment in January, 1924, followed by intense reaction and severe pelvic pain with a loss of 60 pounds in weight. When I saw her in March, 1924 in her home, I considered her a hopeless case in the last stages, with probable involvement of the pelvic bones and pyometra. Three months later she was free from pain, and made a remarkable recovery. She is now, after nearly five years, free from all evidence of the disease, has regained her full weight and strength.

Miss J. (38771) and Mrs. B. (38526) made similar recoveries from apparent hopeless conditions.

b. Repeated Irradiations.—Our monthly inspections have enabled us to discover an early recrudescence or recurrence so that we can apply radium in time to stop the progress of the disease before it has gained headway and given symptoms. We have many examples of this.

Mrs. S. (33196) had 5 such irradiations. She is well after nearly five years. Mrs. O'B. (29692) had 4 treatments, the last in 1924. She is now well after 6 years. Mrs. S. (31244) had her first treatment in October, 1922; lost trace of her for two years, because she felt well. Returned in February, 1926, four years after first treatment, because of spotting. A small area of recurrence reradiated with needles. She has been perfectly well ever since, now five and one-half years. Mrs. W. (33839) had three treatments for recurrences; well since last treatment in November, 1925, now over four years. Mrs. F. (32186) two treatments, last in January, 1924, for recurrence, well now for five years. Mrs. B. (32267) had two treatments, recurrence in November, 1923, perfectly well, five years.

c. One Treatment Only.—In contrast to above cases of repeated irradiations being necessary we have some noteworthy instances of a single application of a moderate dosage resulting in a remarkable result.

Mrs. H. (25377), advanced carcinoma of cervix, Class III-IV. She had one treatment only in March, 1920, of 2400 milligram hours. Neither needles nor x-ray was used. Perfectly well and no evidence of the disease after eight years. A study of the slide shows that the type of cell in this case was of Group I according to Cutler's classification, or the most radioresistant. Mrs. H. (32769), Class II (early). One treatment of 2400 milligram hours, no needles or x-ray. Now well after four years and eight months. Type of cell was Group II of Cutler's classification. Mrs. K. (32130), Class II (early); 3600 milligram hours, now well after five years. The type of cell was Group I of Cutler's classification or *most* radioresistant. Mrs. N. (35053), Class III; 3600 milligram hours, symptom free three and one-half years. Type of cell is Group III of Cutler's classification or *least* radioresistant.

d. Carcinoma of Cervix After Supravaginal Hysterectomy.—We have encountered occurrence of carcinoma in the cervical stump after supravaginal hysterectomy in 11 cases during a period of seven years. Of these only 4 had been operated upon in the Woman's Hospital during which time 872 supravaginal hysterectomies had been done. The incidence is, therefore, probably less than 1 per cent.

Mrs. S. (22599). Supravaginal hysterectomy done on May 2, 1919, pathologic report showed adenocarcinoma involving the cervix. Twenty-four hundred milligram hours' irradiation on May 21, 1919, alive and well after nine years.

e. Irradiation and Subsequent Operation With Microscopic Examination of the Specimen.—We have had the opportunity to examine the uterus after radiation in several cases.

Mrs. T. (31782). Carcinoma of the cervix, Class III, with myoma uteri. Twenty-four hundred milligram hours of radium given in February, 1923, with apparent cure of carcinoma. Three years later, in May, 1926, a panhysterectomy was done because of the large myoma causing pain. The pathologist's report shows that the carcinoma was of the squamous-cell type, Group II of Cutler's classification. The uterus, removed three years later, contained several intramucous and submucous myomas, the largest measuring 12 by 7 by 7 cm. The endometrium was pale and thin. There was no sign of tumor in the hard, pale, shrunk, cervix. Four different blocks, covering the cervix and the lower portion of the body were sectioned. None of them showed any trace of carcinoma. Many slides were examined. Sections from the appendages were also negative. She is well and symptom free, more than five years.

Mrs. R. (23708). Carcinoma of cervix, Class II, with myoma uteri. Twenty-four hundred milligram hours of radium applied in November, 1919. Two months later in January, 1920 a Wertheim operation was done. The pathologic report of the specimen shows the uterus to be enlarged 10 by 6 by 5 cm. The corpus contains a globular myoma of 3 cm. diameter. A broad portion of the parametria and a vaginal cuff of 2½ cm. width are attached to the uterus. The cervix shows deep lacerations and an eroded area on a bulging portion of one lip. About 1 cm. above the external orifice one finds a minute depression which is surrounded by a thick layer of the very hard fibrous tissue. There are no signs of a neoplasm in the cervix. One tube shows a hydrosalpinx of 3 by 10 cm. Microscopically, sections of the lymph glands show no changes. Section of the corpus shows atrophic mucosa. Among several sections of the cervix one finds one section which contains in an inflamed tissue space an oval structure composed of epithelial cells of the small type, but no trace of carcinoma. There are also normal cervical glands on the surface. Section of the ovary shows no oval follicles. On July 12, 1922 in the follow-up two years and six months after the Wertheim operation, a small nodule was observed on the anterior vaginal wall which was suspicious. Two radium needles were implanted on either side of this nodule for thirty-six hours on July 19, 1922, since which time she has been perfectly well, nearly eight and one-half years.

Mrs. P. (23684). Carcinoma of cervix, Class II, of four months' duration. Twenty-four hundred milligram hours of radium in May, 1919. On account of the unusual favorable conditions a Wertheim operation was done in November, 1919, six months later. The pathologic report states the specimen is a somewhat atrophic uterus 7 by 4 by 2 cm. with a thin mucosa. The cervix is lacerated, a vaginal cuff of 2 cm. width and a large amount of parametrial tissue is attached to the uterus. On either side of the cervical canal between the external and internal os are two lenticular projections from the mucosa ½ cm. in long diameter. These are firm fibrous and white on section and appear sharply denuded from the cervical stroma. Microscopic sections of the entire uterus show these areas to be dense cicatricial tissue sharply limited from the cervical stroma. They contain a few nuclei and are largely hyaline collagen fibrils. The remainder of this cervical stroma is rather dense and cellular. There are some dilated cervical glands but the mucosa is largely atrophic. Mucosa of the corpus uteri is thin, shows few glands which are of the

interval type and somewhat atrophic. Myometrial tissue throughout the corpus and fundus shows no changes. No section shows any trace of the original carcinoma. Unfortunately we have lost trace of this patient because she returned to her home in Spain. Our last account was two years after her treatment when we heard she was very well. This case is of especial interest because it has afforded us the opportunity to study the effects of a single application of radium on an early carcinoma of the cervix, and the very thorough sectioning of the entire specimen by Dr. Strong reveals no trace of cancer cells remaining six months later. Apparently the Wertheim operation was unnecessary in this case, and it affords a justification for the use of radium instead of operation in the disputed frankly early cases.

f. *Pyometra and Hematometra the Result of Postradiation Contraction.*—The occurrence of pyometra or hematometra as a post radiation complication we believe is an important factor to be remembered, because we have observed in our follow-up many instances of an apparent extension of the carcinoma as evidenced by increase in the size of the uterus and marked pelvic pain and temperature that on investigation proved to be a retention of purulent or bloody fluid in the body of the uterus as a result of stenosis of the canal following the contraction from irradiation. The passage of a sound will at once clear up the diagnosis and an occasional passage of dilators will suffice to correct this complication. We have several instances, where a hopeless prognosis was given, that are now alive and well, as the trouble was due to this condition and not to an extension of the disease.

Mrs. S. (33196). Carcinoma cervix, Class II, intracervical in location, from November, 1923 to November, 1925, she had four reradiations for recurrence, following the initial treatment. In October, 1925 a condition of pyometra was discovered which accounted for an acute condition. Divulsion and irrigation resulted in the evacuation of much slough and pus and a satisfactory cure, as she is now alive and well.

Mrs. K. (32130). Carcinoma cervix, Class II. Thirty-six hundred milligram hours in April, 1923. One year later symptoms of apparent extension of the disease, which proved to be pyometra. She was divulsed and irrigated and has been perfectly well ever since, now five years.

Undoubtedly the automatic evacuation of a pyometra accounts for the sudden improvement in the toxic condition of some of these patients which has led us to believe them to be hopeless cases.

g. *Postradiation Hemorrhage.*—We must expect the possibility of hemorrhage at the time of the separation of the slough resulting from irradiation. Usually this is not marked but occasionally it may be severe, requiring prompt packing and transfusion.

Mrs. S. (38462). Carcinoma cervix, Class II. Two irradiations, the last August 13, 1927. On October 19, 1927, she had a severe hemorrhage and was taken to the hospital for treatment. Today she is free from all symptoms.

h. *Fistulae.*—The occurrence of fistulae is an unfortunate complication of irradiation, although it is difficult to say whether the fistula develops as a result of the therapy or the disease. Both are undoubt-

edly factors in some instances. As our experience increases in the application of radium we should expect a decreasing percentage of these sequelae. In 196 cases we had 9 cases with fistulae. Our experience has been that the rectovaginal fistulae will tend to heal spontaneously, while the vesicovaginal will persist but may be closed by operation.

In the case of Mrs. B., previously referred to as with rectovaginal and vesicovaginal fistulas and now alive and free from symptoms of carcinoma after eight years and ten months; the rectovaginal fistula healed spontaneously.

Miss J., aged thirty years. Carcinoma cervix, Class III. Three thousand six hundred milligram hours of radium given on February 7, 1927. June 7, 1927, she was in a very bad condition and was referred to House of Calvary as hopeless. November, 1927, well with no evidence of carcinoma but has a vesicovaginal fistula, circular in shape about 2 cm. in diameter at the cervicovaginal junction in a nulliparous vagina. As a rule we have avoided operation in these cases fearing that the dissection might liberate some imprisoned dormant cancer cells and disseminate them, but at the urgent request of the patient whose condition was intolerable, we operated last February and fortunately were successful in closing the fistula.

i. *Carcinoma of Fundus*.—While it is generally agreed that panhysterectomy gives a sufficiently high percentage of five-year cures in carcinoma of the fundus, yet in our experience we have not been able to operate in over 50 per cent of our cases because of the poor surgical risk. These patients are frequently advanced in years, and complicated with obesity, cardiovascular disease, deficient renal function, or diabetes. We have, therefore, had to resort to radium therapy alone in such cases. Our method of choice is first to apply radium to the body of the uterus and later do a panhysterectomy.

Heyman's report shows that the result in operable cases from several clinics gives a cure in 58.8 per cent, while the Radium-hemet with radiologic treatment alone has 60 per cent. Our figures have not been completed to date, but in a previous report approximated those quoted by Heyman. It is our custom to resort to a diagnostic curettage when the diagnosis is in doubt in suspected fundus carcinoma. An instance of repeated failures of the curettage to determine the diagnosis is possible.

Mrs. B. (36306), seventy years old, had suspicious symptoms and was curetted twice with negative findings; as the symptoms continued, a third curettage was done with positive finding of adenocarcinoma.

Mrs. R. (25917), very obese and poor surgical risk. Adenocarcinoma of fundus, 2 tubes 50 milligrams in tandem were applied for thirteen hours in June, 1920. On account of a recurrence of symptoms, a second irradiation was given for twenty hours in December, 1921. In November, 1925, needles were implanted in a metastasis on the anterior vaginal wall. She is now symptom free after nearly eight years, showing what may be done in a poor risk by repeated irradiation.

Mrs. H. (30640). Adenocarcinoma of fundus. Two thousand four hundred milligram hours of radium to fundus in June, 1922. In January, 1923, the uterus was

smaller and mobile, but there was still some discharge. A panhysterectomy was done and the pathologic report shows active adenocarcinoma in the cavity. This illustrates the advisability of operating wherever possible, as this patient has been alive and well for nearly six years.

Mrs. P. (25265), aged sixty-five years. Adenocarcinoma of fundus. Two thousand four hundred milligram hours of radium in February, 1920. A panhysterectomy was done one week later and a second application of 1500 milligram hours of radium to the vaginal vault was made twenty-five days after the operation. The patient had marked vesical irritability for some weeks after the second irradiation but made a good recovery. The subsequent history is interesting. In 1921 she had a mild stroke, but recovered. In 1925 she was married. In 1926 she had a second stroke from which she recovered. She is now well and happy at seventy-three years of age after eight years.

PROGNOSIS FROM THE TYPE OF CELL

In view of the interest that has been aroused by Martzloff, Cutler and others on the possibility of making a prognosis as to the probable reaction to irradiation in accordance with the predominating type of cell in cervical carcinoma, I have had Dr. Plaut, our pathologist, study the type of cell in this series of outstanding results that I have given as examples.

In 23 of this group, excluding the adenocarcinomas, the distribution in accordance with the classification of Cutler is as follows:

Group I (adult)—5 cases (most radio resistant)—22 per cent.

Group II (plexiform)—16 cases (intermediate)—69 per cent.

Group III (anaplastic)—2 cases (least radio resistant)—9 per cent.

Cutler's average of distribution in 200 cases was Group I 17.5 per cent, Group II 61.5 per cent, and Group III 21 per cent. Dr. Plaut states, "Looking for an explanation of the favorable result of radium therapy in these cases, remarkable from the clinical standpoint, we cannot find it in the histologic group according to Cutler. Among the 23 favorable cases there is no higher percentage of the anaplastic tumors (Group III) which are supposed to give the best results with irradiation, and the percentages of the highly differentiated tumors (Group I) which are expected to give a poor result with irradiation is even higher than the average given by Cutler for all cases."

While we hope that the grading of the type of cell may prove to be as reliable an index of prognosis as some pathologists expect, still we are inclined to believe with Plaut that there is at present a bewildering mass of contradictory evidence as to its value.

PROPHYLAXIS

The rôle of chronic irritation as an etiologic factor in the development of carcinoma makes it imperative that lacerations and erosions of the cervix should not be neglected. In a study by Farrar of 300 consecutive case histories of cancer of the cervix at the Woman's Hos-

pital, it was found that pregnancy had occurred in 96 per cent. In 288 cases 11.1 per cent of the patients had had the last pregnancy less than five years and 20.3 per cent less than ten years before entering the hospital for the malignancy. We believe that the immediate repair of cervical lacerations when done under proper conditions, as in a hospital, will lessen the danger of subsequent development of carcinoma in the cervix.

DANGER OF THE USE OF RADIUM BY THE INEXPERIENCED

We wish to sound a warning as to the real danger of the indiscriminate application of radium by those inexperienced in its use. Commercial organizations exploiting radium send broadcast alluring literature offering to any physician advice and facilities as to dosage and technic on receiving the history of a case. We know of several instances of serious permanent damage being done through the careless and ignorant application of radium by those not qualified.

A recent case occurred in a young woman, aged twenty-seven years, who had one child delivered at the Woman's Hospital four and one-half years ago. A year later, in another city, she was given radium treatment because of menorrhagia. The radium was kept in situ for *three days and ten hours* with severe reaction and invalidism. She now has a small atrophic uterus and senile vaginitis with marked menopause symptoms and is anxious for another child.

Expert experience is necessary to obtain the best results and to avoid harm.

CONCLUSIONS

In conclusion I wish to draw attention to the following creed which I hold.

There is less primary mortality, less morbidity, less loss of time with radium therapy than in the radical operation for carcinoma of the cervix.

The palliative results in cases not permanently cured are an important advantage, not to be ignored.

The morbidity results of the radical operation, fistulas, thrombosis, suppuration, etc., are not to be forgotten.

Vesical and rectal fistulas should be increasingly less frequent in radium therapy as the technic develops.

Repeated irradiations are of distinct value, and subsequent treatments should be based on the reaction to the initial or test dose.

A personal monthly inspection or follow-up is an essential throughout the period of observation, in order that by a watchful waiting we may discover a recurrence in its incipency and thus extinguish the fire before it has gained headway.

We should be careful not to give a positive unfavorable prognosis until *after* the sloughing stage has terminated, and we should watch out for pyometra.

Large amounts of radium are not necessary to produce results.

There is a great need for the standardization of our statistical reports.

The immediate repair of cervical lacerations is a valuable prophylactic measure.

We believe that our results show that radium is preferable in all classes of cervical carcinoma. We also believe that in the very early cases the radical operation will give the same result as radium, *but* at the cost of high primary mortality and greater morbidity.

We agree with Polak's statement that all borderline cases fall within the range of radium and not operation.

As to the early cases—and how few we see—with the present statistical figures available, it is not yet proved which gives the best results, but the available figures do *not* show that the operation is any better than radium.

48 EAST FIFTY-SECOND STREET.

(For discussion, see page 126.)

CHANGES IN THE LEUCOCYTES DURING LABOR AND THE PUERPERIUM

A REVIEW OF THE LITERATURE AND AN ANALYSIS OF FIFTY-FIVE CASES

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BUT little attention has been given to the changes in the leucocytes during labor and their possible significance. Other than to mention that leucocytosis occurs during labor, the textbooks on obstetrics hardly consider this subject. It was thought, therefore, that a complete survey of the literature together with an independent investigation might prove of interest to those who desire specific information of this nature, even though the study does not reveal facts of clinical value.

PREVIOUS INVESTIGATIONS

Hibbard and White¹⁹ made total white blood cell counts in 55 cases of labor and differential counts in 19 cases. In 75 per cent of all the cases, and in 84 per cent of primiparae, they found leucocytosis during labor. The average white blood cell count for primiparae was 15,021; for multiparae, 11,700. When the total white cell count was normal, the differential count also was unchanged. However, in the patients with leucocytosis, there was both a relative and an absolute increase in the polymorphonuclear neutrophils, while the lymphocytes were relatively decreased with normal or diminished absolute values.

Habl¹⁶ confirmed the findings of Hibbard and White with respect to the degree of leucocytosis during labor. In a series of 36 cases, the average white blood cell count was 15,380 for primiparae; 12,940, for multiparae. Furthermore, the leucocytosis was due to both a relative and an absolute increase in the polymorphonuclear cells. When leucocytosis reached its peak, the eosinophiles were decreased both relatively and absolutely.

Carton⁷ reported the total and differential counts in 10 primiparae and in 10 multiparae. During labor the number and percentage of neutrophils were increased, while the eosinophiles were either absent or greatly diminished. There was a rise in the eosinophiles and mononuclear cells during the puerperium, keeping pace with the drop in the polymorphonuclears. In cases of puerperal infection, the absolute number and percentage of the polymorphonuclears remained persistently high.

Birnbaum⁴ likewise observed leucocytosis with a relative and absolute increase in the neutrophils during labor. Primiparae averaged 92 per cent neutrophils; multiparae, somewhat less. Except in cases of infection, normal differential values were established by the fourteenth day postpartum.

Arneth^{1,2} found a leucocytosis over 10,000 in all but one case of a series of eight, including six primiparae and two multiparae. When the Arneth count was done, a definite shift to the left was found; that is, the polymorphonuclear cells of Groups I and II of the Arneth formula were increased at the expense of those of the remaining three groups. In one case in which the total leucocytes remained at the normal level of 8,000, the percentage of neutrophils in the Arneth Group I was 34 per cent, the normal being only 5 per cent.*

Pankow²⁴ found an increase in the total leucocyte count during labor, which persisted for a few hours after the delivery of the placenta and then declined, often quite rapidly, if there were no complications.

Given¹⁴ obtained counts during the first stage of labor or within twenty-four hours of delivery which largely confirmed the work of earlier observers. He noted leucocytosis with both a relative and an absolute increase in the neutrophils and a corresponding fall in the lymphocytes, followed by a rapid rise of the latter cells during the puerperium. He found, however, but slight change in the percentage of eosinophiles; whereas most observers have noticed a pronounced drop in these cells during and immediately following labor.

Blumenthal^{5,6} found the polymorphonuclear leucocytosis during labor to be due to an increase in the number of young forms; that is, there is a shift to the left by the Arneth count. When the count was made after rupture of the fetal membranes, the degree of leucocytosis was lessened and the eosinophiles practically disappeared. After separation of the placenta, leucocytosis was more marked than during the first stage. At this time, Blumenthal found the polymorphonuclears much increased, the mononuclears diminished both relatively and absolutely, the eosinophiles absent, and an increase in the younger forms of the neutrophils. After labor the differential count returned to normal and the eosinophiles reappeared.

Horvath²⁰ found that the leucocytosis of labor reaches its peak in from three to seven hours after delivery. The lymphocytes are decreased relatively but not absolutely. He noted a disappearance of the eosinophiles during labor and an Arneth shift to the left, the neutrophils of the Arneth Groups IV and V being considerably diminished.

Dietrich¹⁰ observed that the increase in the white blood cell count begins with the onset of labor pains and continues throughout labor and for some hours afterward. In 16 of 19 cases, the eosinophiles and basophiles disappeared entirely; but

*References 15, 23, 29, 30 were included in the original text, which has been shortened for lack of space. These references, however, are of importance, and I have left the original numbers as changing them would mean changing type numbers through the entire article.

the eosinophiles reappeared by the end of the first day. The normal differential count was reestablished by the third day.

Doi¹¹ reported 28 cases in which the findings confirmed those of earlier observers with regard to the degree of leucocytosis and the changes in the neutrophiles, lymphocytes, eosinophiles, and Arneth count. He found that the longer the duration of labor, the more gradual was the return to normal in the total count. However, a normal reading was always obtained after twenty-four hours in uncomplicated cases. In the early days of the puerperium the small lymphocytes tend to increase, the large lymphocytes, to decrease.

Sieben²⁸ noted a disappearance of the eosinophiles in 50 per cent of cases during labor. In some instances there was an absolute decrease in the lymphocytes. The mononuclears, basophiles, and transitionals were reduced after labor; often they were entirely absent.

Chamorro⁸ found an average of 75 per cent of polymorphonuclear cells in the blood of primiparae during pregnancy. At parturition the average was 22.66 per cent of small lymphocytes, 3.13 per cent of mononuclears, and only 0.01 per cent of eosinophiles; the transitional cells were normal, that is 1 per cent. In multiparae, the average polymorphonuclear count was 83.66 per cent, and the lymphocytes underwent a marked reduction, averaging 14 per cent.

Baer³ made an exhaustive study of the leucocytes in pregnancy, labor, and the puerperium, basing his observations on 100 cases in which the counts were taken during labor and once daily thereafter for ten consecutive days. Primiparae showed a higher leucocytosis than multiparae, the average total count for 30 primiparae being 18,255 during labor with the high point, 19,883, on the first day of the puerperium and a gradual reduction after that. The average among 57 multiparae during labor was 13,467, with the high point, 15,062, on the first day of the puerperium. With each successive labor, there seemed to be a decreased reaction on the part of the leucocytes.

During labor the average differential counts in the 30 primiparae was 83.2 per cent neutrophiles, 10.8 per cent small lymphocytes, 3.5 per cent large lymphocytes, 1.7 per cent eosinophiles, 0.3 per cent transitionals, and 0.5 per cent mast cells. On the first day of the puerperium, the counts were as follows: 81.7 per cent neutrophiles, 10.3 per cent small lymphocytes, 3.5 per cent large lymphocytes, 3.0 per cent eosinophiles, 0.1 per cent transitionals, and 0.4 per cent mast cells.

During labor the average differential count in 57 multiparae was 77.7 per cent neutrophiles, 16.3 per cent small lymphocytes, 4.1 per cent large lymphocytes, 0.5 per cent eosinophiles, 0.6 per cent transitionals, and 0.8 per cent mast cells. On the first day of the puerperium, the average count was as follows: 79.2 per cent neutrophiles, 12.8 per cent small lymphocytes, 5.3 per cent large lymphocytes, 1.1 per cent eosinophiles, 0.8 per cent transitionals, and 0.8 per cent mast cells. The eosinophiles were entirely absent during labor in about half the cases of this series, reappearing in normal proportions on the first day postpartum.

In summarizing the findings the author stated: "Differential analysis showed the increase in leucocytes to be chiefly in the polymorphonuclear neutrophiles with a return to normal proportions by the third day of the puerperium, an absence of eosinophiles in about half the cases in labor, and their reappearance in normal proportions on the first day of the puerperium. . . . The small lymphocytes were diminished as the polymorphonuclear leucocytosis increased, and the large mononuclear, transitional forms and mast cells maintained normal percentages." Baer also noted that the Arneth analysis showed a displacement toward the left, i.e., toward Classes II and III; but this was not constant.

Jerlov's²¹ observations helped to corroborate existing views with regard to the number and percentages of the leucocytes during labor and the puerperium. In 19 cases studied immediately after delivery, the average count was 16,055, 14,220 of which were neutrophiles. Polymorphonuclear leucocytosis was somewhat more

marked in primiparae than in multiparae. The lymphocytes were diminished in absolute numbers, averaging 939 cells. Disappearance of the eosinophiles was observed by Jerlov, as by other investigators. In complicated cases, neutrophilic leucocytosis persisted and the eosinophiles failed to return at the usual rate, particularly in cases of infection.

As recent writers on the subject have utilized the Schilling hemogram in studying their differential blood counts, it is necessary to refer in some detail to this diagnostic method.

According to Schilling^{26, 27}, the normal total leucocyte count is 6,000 to 8,000. For the differential count he classifies the leucocytes as follows: basophiles; eosinophiles; neutrophiles, including four classes—myelocytes, immature cells, cells with rod-shaped nuclei, and cells with segmented nuclei; lymphocytes; and monocytes. The total and differential count is shown by a "hemogram," in which the following abbreviations are used for the different types of leucocytes:

B—basophiles; E—eosinophiles; neutrophiles; M—myelocytes, J—Jugendliche (immature cells), St—Stabkernige (rod-shaped nuclei) and S—Segmentkernige (segmented nuclei); L—lymphocytes; Mon—monocytes.

The hemogram shows the percentage of each type of leucocyte. The normal hemogram is given by Schilling as follows:

NUMBER OF LEUCOCYTES	B	E	M	J	ST	S	LY	MON
6000-8000	1	3	—	—	4	63	23	6

J (immature cells) may be present in normal blood up to 1 per cent. Myelocytes are not present in normal blood.

Fuss¹³ found that the neutrophilic cells show a definite displacement to the left in Schilling's hemogram during labor. This change is most marked in primiparae without complications. In the puerperium the displacement to the left tends to disappear, unless there is some complication. The neutrophiles react promptly to any complication with a renewed shift to the left. In sepsis Fuss states that the immature forms (J) and the myelocytes (M) show unusually high percentages.

The blood picture in labor, according to Fuss, is characterized by the following: a displacement to the left of the neutrophilic leucocytes, sometimes with very high percentages of those with the rod-shaped nuclei (St); disappearance of the eosinophiles; diminution of the lymphocytes, often with a rapid fall in their count; and diminution of the large mononuclears. From the second day of the puerperium in uncomplicated cases, there is a tendency for the blood picture to return to normal.

The observations of Saidl and Tuma²⁵ helped to corroborate previous work on the subject. In their experience, based on observations on 104 childbearing women, the differential values vary greatly in pregnancy, labor, and the puerperium. The leucocytosis is due especially to an increase in the neutrophiles. In multiparae, leucocytosis is less common. At the beginning of labor, there is an increase of neutrophiles. In the puerperium, the number of neutrophiles drops again, while the lymphocytes are increased. The neutrophilia is also associated with a slight displacement to the left. Contrary to most observers, Saidl and Tuma did not observe a diminution of the eosinophiles during labor.

Heyn¹⁸ employed Schilling's hemogram for differential counts in 20 cases during the last week or two of pregnancy, during labor, and postpartum. Of these 20 patients, 14 were primiparae and 6 were multiparae. The hemograms showed an increase in the polymorphonuclear percentage and a diminution in the percentage of lymphocytes with but slight absolute decrease. A definite displacement to the left of the polymorphonuclears in the Schilling hemogram was noted. In 3 cases,

a few myelocytes were present. Eosinophiles were found in only 6 of the 20 cases, and then in small percentage.

In the puerperium, the leucocytosis noted during labor diminished progressively in uncomplicated cases, often quite rapidly. The rapidity of the decrease in the white cell count postpartum was proportional to the rapidity of the increase during labor. The diminution in the total leucocyte count was accompanied by a diminution in the percentage of the polymorphonuclear neutrophiles and a disappearance of the displacement to the left. The relative lymphocyte count often increased rapidly. This relative lymphocytosis persisted in several cases during the period of lactation.

Crawford⁹ noted leucocytosis during labor in 50 Chinese women, averaging 14,100 cells. The count rapidly fell after labor. Maxwell and Yang²² confirmed this finding in a study of 10 childbearing Chinese women. The average count during labor in their cases was 15,175, reaching a peak of 17,960 within twenty hours. They also noted an increase in the percentage of neutrophiles and a diminution in the lymphocytes during labor, but disappearance of the eosinophiles occurred in only two of their cases.

Würzburger³¹, utilizing Schilling's hemogram, noted slight leucocytosis in some cases in the last days of pregnancy, an increase in the white cells immediately after labor, a return to normal in the puerperium, and a displacement to the left in the neutrophiles after labor. Any complication in the puerperium interfered with the return of the blood picture to normal. Würzburger gave the accompanying figures as average hemograms in the latter part of pregnancy, immediately after labor, and in the puerperium, respectively:

	TIME	LEUCOCYTE								
		COUNT	B	E	M	J	ST	S	L	GR. M.
1	In pregnancy	8,900	—	—	—	5	18	56	20	1
2		9,400	—	—	—	7	20	50	23	—
3	Immediately after labor	9,300	—	—	—	10	20	45	25	—
4		10,100	—	—	—	8	11	60	21	—
5	In puerperium	7,800	—	—	—	5	8	68	19	—

Haeusermann¹⁷ made differential leucocyte counts according to Schilling's hemogram in 120 normal labors, 7 cases of eclampsia, 6 of preeclampsia, and 2 of puerperal fever. He found no absolutely characteristic hemogram during labor, especially in multiparae. There was usually a diminution in the eosinophiles, which disappeared entirely in some cases, especially in primiparae. Myelocytes were never found, and immature cells were rare. The neutrophiles with rod-shaped nuclei were usually increased, but occasionally diminished. There was, as a rule, a definite increase in the cells with segmented nuclei. The lymphocytes were often so much diminished that it could be said that there was a lymphopenia. This was not invariably the case, as occasionally the lymphocytic percentage was almost normal. Haeusermann found a tendency to displacement to the left in the hemogram during labor, but it was not so marked as in the cases reported by Fuss. He believes that this displacement to the left is of no significance in labor, and in normal cases it decreases or disappears by the second or third day postpartum. If it persists or increases, it indicates some complication. If the eosinophiles reappear and the lymphocytes increase in cases with postpartum fever, even though displacement to the left persists, Haeusermann maintains that it indicates a benign process. In a case of fatal puerperal infection, the hemogram showed absence of eosinophiles, appearance of a few myelocytes, increase in immature cells and cells with rod-shaped and segmented nuclei, and diminution in the lymphocytes. In eclampsia, there was always a definite displacement to the left in the hemogram with an increase in the immature cells and cells with rod-shaped nuclei, which condition disappeared after delivery and cessation of the eclamptic attacks.

REPORT OF PRESENT STUDY

In 55 cases of labor, routine differential counts of the white blood cells were made on six different occasions; namely, (1) on admission; (2) just before delivery, that is, from fifteen minutes to one hour before the birth of the child; (3) just after delivery, that is, from fifteen to thirty minutes after the birth of the child; (4) twenty-four hours after delivery; (5) five days after delivery, and (6) ten days after delivery.

The blood smears were taken by the intern in each case and stained by an expert hematologic technician. The stains used were Wright's and Giemsa's. For each count, the technician enumerated 400 cells. His work was personally supervised.

TABLE I. AVERAGE DIFFERENTIAL BLOOD COUNT IN TWENTY-THREE NORMAL CASES

	POLY- MOR- PHONU- CLEARS	SMALL MONONU- CLEARS	LARGE MONONU- CLEARS	EOSINO- PHILES	BASO- PHILES	TRANSI- TIONALS
ADMISSION	75.0	21.0	2.7	0.06	0	0.91
Just before delivery	78.6	18.1	2.2	0.02	0	0.94
Just after delivery	77.8	19.7	2.2	0.04	0	0.86
24 hours after	76.4	19.8	2.4	0.33	0	1.02
5 days after	73.9	21.7	2.6	0.83	0	0.91
10 days after	72.3	23.2	2.6	0.99	0	0.83

For the sake of convenience, I have divided the cases studied into three groups; namely, (1) normal cases, (2) abnormal cases, and (3) a small group of five cases, in which total leucocyte counts were made as well as the differential counts.

Twenty-three cases of normal labor were studied with respect to report of the results, but an average of the total figures is given in Table I.

the differential blood counts. Space does not permit of a detailed report. Feinblatt and Eggerth¹² give the following figures as normal values for the differential white cell count:

Polymorphonuclear neutrophiles	62.0 to 70.0 per cent
Lymphocytes	20.0 to 30.0 per cent
Large mononuclears and transitionals	4.0 to 8.0 per cent
Eosinophiles	1.0 to 3.0 per cent
Basophiles (mast-cells)	0.2 to 0.6 per cent

By comparing the figures given in Table I with those furnished by Feinblatt and Eggerth, it will be noted that the percentage of neutrophiles rises before labor and stays at a high level during the first day postpartum, gradually subsiding during the puerperium. The small lymphocytes, or small mononuclear cells, decrease in inverse proportion to the polymorphonuclear cells; that is, their percentage drops before delivery and gradually returns to normal during the puerperium. The eosinophiles are markedly diminished just before and after delivery. They do not approach normal values until late

in the puerperal period. At no time were any mast-cells found in any of my 23 normal cases. This is rather a remarkable observation, inasmuch as 400 cells were counted in each instance.

Twenty-seven abnormal obstetric cases were studied, but the findings were not sufficiently consistent to allow of definite conclusions. Of course, when infection is present, the total number of leucocytes and the percentage of polymorphonuclear cells are increased. Normally the eosinophiles do not reappear until several days after labor. In complicated cases, this reappearance may be delayed for several days or longer. With the least rise of temperature or the presence of any complication, the percentage of small lymphocytes is diminished; this change probably results from the increased number and percentage of neutrophiles formed in these conditions. In patients with cracked nipples, a lump in the breast, or slight abdominal tenderness, a slight fall in the small lymphocyte count was not uncommon.

SUMMARY

A study was made of the changes in the differential white blood cell count during labor and the puerperium. My findings in a series of 55 deliveries, 23 of them normal cases, merely serve to corroborate those of earlier investigators, whose work I have summarized in a comprehensive review of the literature. During labor and the first day or two postpartum, there is a moderate grade of leucocytosis, which reaches its peak several hours after delivery. The polymorphonuclear cells are increased both in relative and in absolute numbers. There is a slight percentage decrease in the small lymphocytes, which is usually inversely proportional to the percentage of neutrophiles and regains the normal value at about the same time. The eosinophiles and basophiles are notably absent or greatly diminished during labor. In the absence of complications, the eosinophiles begin to reappear by about the third day of the puerperium. The neutrophiles show a marked shift to the left by the Arneth count and also in Schilling's hemogram.

Except for the established fact that the percentage of polymorphonuclear cells is increased in infections, the differential count would appear to be of little value in labor and the puerperium. It has been observed that the eosinophiles do not appear until several days or more after the third day in complicated cases; that the percentage of lymphocytes is usually still further diminished in the presence of fever or other complications, and that even such slight complications as a cracked nipple, a lump in the breast, or slight tenderness in the abdomen may cause a slight reduction in the percentage of lymphocytes.

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303 WEST ONE HUNDRED AND SIXTH STREET.

DRY LABOR

AN ANALYSIS OF 600 CASES

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PREMATURE rupture of the membranes is a complication of labor which is very generally feared. A frequent occurrence in dystocia, it has come to be considered in itself a very important cause of dystocia as well as a serious menace to both mother and child from ascending infection. Yet every obstetrician of experience has seen many cases in which rupture of the membranes before the onset of pains was followed by a very rapid easy labor without untoward results for either mother or child.

To determine the true prognostic significance of this complication, the factors resulting in difficulty, and the outcome under various forms of treatment, we have studied the cases of dry labor in a series of 6500 deliveries on the University of California Obstetrical Service. In order to secure as clear a picture as possible of the effects due definitely to the premature rupture, we have included only those cases in which rupture occurred with or before the onset of pains, and have included all such cases no matter how rapidly labor was completed. Our study indicates that an arbitrary time limit, such as that of

twelve hours or more between rupture and delivery, as taken by Dorman and Lyon, may give a false idea of prognosis, since it eliminates a large proportion of patients with premature rupture who complete labor without difficulty in much less than this time, while it includes many patients in whom rupture early in the course of a long labor may be only a minor factor in dystocia due to other causes.

Under our classification are included 604 cases of dry labor occurring after the fetus had reached the age of viability, or 9.3 per cent of the total series.

Etiology.—In considering etiologic factors, we find that primiparity seems to predispose to the condition, as the incidence in primiparae was 12.34 per cent, while in multiparae it was only 7.1 per cent. This confirms a similar observation of Dorman and Lyon.

The age curve of the two types of patients is shown in the accompanying graph. (Fig. 1.)

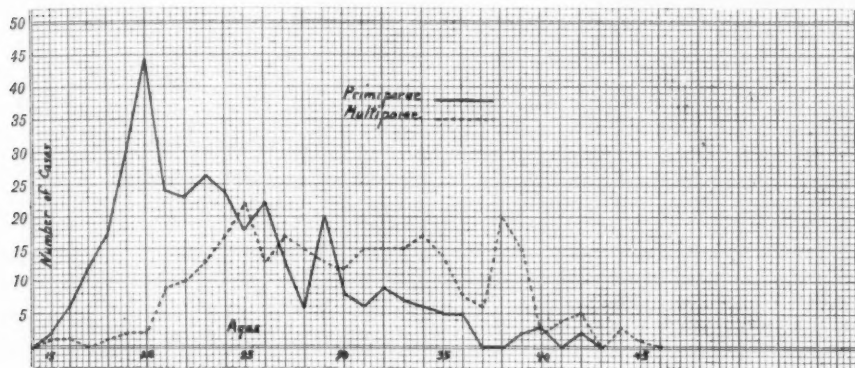


Fig. 1.

The ages of the primiparae varied from fifteen to forty-two years, with a rapid rise in the curve to the greatest number at twenty followed by a rapid fall. The multiparae varied from fifteen to forty-five years, with the greatest number at twenty-five, but with a much more uniform distribution over the various ages. As this corresponds very closely to the average age incidence in the two types of cases, it does not confirm Bassett's contention that the condition occurs most frequently in young primiparae and old multiparae.

Eight per cent of the cases were delivered a month or more before term, and 23 per cent two weeks or more; yet since rupture of the membranes is followed by termination of the pregnancy in a comparatively short time in practically all cases, it is probable that prematurity is a consequence rather than a cause of the premature rupture. The average weight of the children was 3196 gm., considerably below the 3478 gm. average weight in a series at term reported from this clinic by Maxwell.

On the other hand, the proportion of overlarge children and of twin pregnancies was much greater than usual, indicating that overdistention of the uterus may be a causal factor. Eight and six-tenths per cent of the children weighed over 4000 gm., while the average incidence of children of this weight was 4.3 per cent. There were 15 twin pregnancies, or 2.5 per cent, more than three times the incidence in the total series (0.78 per cent).

Although rupture of the membranes early in labor is very frequent in contracted pelvis, the condition apparently does not predispose to rupture before the onset of pains, as the incidence of contracted pelvis in this series of dry labors was 3.9 per cent—exactly the same as that found by Maxwell in the total series of 6500 cases.

Abnormal presentations, however, were of considerable importance, as breech presentation occurred in 6.1 per cent of the cases, or 7.1 per cent if we include those in twins, while they formed only 2 per cent of the total series. There were 14.2 per cent of occipitoposteriors, while these formed only 10 per cent of the total. There were also 3 transverse and 2 face presentations.

Lack of engagement of the head would seem to be a factor of probable importance, and an attempt was made to determine this point. This was, however, unsatisfactory, as comparatively few of the patients were examined at the time of rupture of the membranes. Thirty-four per cent of the primiparae, and 39 per cent of the multiparae in whom the point is definitely recorded did show a floating head at the time of the first examination. A patulous cervix has been mentioned as a cause, but if this were a factor of much importance, we would expect dry labor to be more common in multiparae than in primiparae, rather than the reverse. It was recorded in a few cases, but as many of the patients entered in labor with partial dilatation of the cervix, it could not be determined in most of them.

In addition to the mechanical factors, or in their absence, variations in tensile strength of the membranes themselves due to changes in their histologic structure are undoubtedly of the greatest importance. A deficient development of the connective tissue layers, particularly the firm subamniotic connective tissue, as described by Niderehe, and in certain cases by Naujoks, seems the most probable explanation, although the various degenerative changes noted by Naujoks may be of importance also. The changes in the amniotic epithelium described by Heinlein are more likely secondary to reduction in size of the amniotic cavity following loss of amniotic fluid and retraction of the uterus. Inflammatory changes in the membranes are described by numerous authors, and were considered by von Franque, Schmidt, and others due to an extension from an endocervicitis or an endometritis, and leading to premature rupture through an increased friability of

the tissues. The frequent occurrence of premature rupture in primiparae, without history or evidence of infection, is a strong argument against this theory, and in the light of recent research by Slemmons and others, it seems more probable that these inflammatory changes are secondary to the premature rupture and due to bacterial invasion of the amniotic cavity in the course of a prolonged dry labor.

Onset of Pains.—Following premature rupture of the membranes, we find that labor pains begin very shortly in the large majority of cases. Two hundred and twenty-four patients developed pains immediately, and an additional 79 within the first hour; that is to say, more than half the patients began labor within an hour after the membranes ruptured. Only 57, or less than 10 per cent, delayed more than twenty-four hours, and of these more than two-thirds were premature. The average weight of the children where pains were delayed for twenty-four hours or more was 2877 gm. In 13 patients, or 2 per cent of the total, pains were delayed more than three days; in 5 for four days; 2 each for five, six, and seven days; 1 for seventeen days, and 1 for nineteen days. Only 2 of these were term children, 1 on the fourth, and one on the sixth day. The patient who delivered in nineteen days was a twenty-one-year-old primipara who was due on August 3. Her membranes ruptured on July 3; she was seen daily in the clinic and showed a profuse drainage but no signs of infection. On July 22, she fell into labor and after ten hours was delivered of a 2750 gm. child. Her puerperium was afebrile and the child did well.

Induction of Labor.—Castor oil and quinine were given to induce labor after the membranes had ruptured in 50 cases. In one case, quinine and strychnine were used; in 2 cases castor oil alone. The medication was started from one-half hour to five days after the time of rupture, and labor was induced in all but 2 of these fifty patients. Pains began in from one quarter of an hour to fifteen hours, the average time being four hours. In one case unsuccessful on first attempt, castor oil and quinine were first given five days after the membranes ruptured, and were followed only by intestinal cramps. Five days later a second attempt was likewise unsuccessful. Six days after this a Watson routine was ordered, and pains began after the second dose of pituitrin. The labor lasted only two hours. The child was a macerated syphilitic premature. In the other case castor oil and quinine were begun twenty-two hours after the rupture of the membranes. No pains followed; twenty hours later a Voorhees bag was inserted and labor began immediately. A live child was delivered spontaneously in ten hours.

Castor oil and quinine were given to induce labor and were followed by premature rupture of the membranes in 29 cases. The interval between the medication and the premature rupture varied from

two to twenty-four hours, the average being nine and four-tenths hours. In 15 cases, labor began immediately; in the remainder in from one to twenty-three hours, the average being ten hours, except in 4 cases. In one of these castor oil and quinine were followed by rupture of the membranes, but there were no pains. Two days later, a second course of castor oil and quinine was given and was followed by pain in one and a half hours. In a second case, rupture of the membranes occurred four hours after the castor oil and quinine, and irregular pains began immediately and continued for two days without accomplishing delivery. A second dose of castor oil and quinine was then given; pains improved in character, and delivery was accomplished in ten hours. The 2 other cases ruptured their membranes after castor oil and quinine and when no pains had developed, a Voorhees bag was inserted seven and nineteen hours respectively after rupture, and pains began immediately.

Castor oil and quinine, or in a few cases the oil alone, was given during labor in 27 cases. In some cases it was given at the beginning of labor when pains were present but slight and indefinite, in others during the course of a long labor with poor pains, in the hope of stimulating contractions. The results were more satisfactory in the former type of case, and a number developed strong contractions and completed labor promptly.

In view of much recent discussion of possible injurious effects of quinine upon the fetus, it is interesting to note that quinine had been used in only 3 cases in which the fetus was stillborn. As one of these was an anencephalic child, another a macerated premature which showed definite anatomic lesions of syphilis and a luetic placenta, and the third, a severe dystocia in which a destructive operation was finally necessary, it does not appear that the quinine could have been in any way responsible for any of the fetal deaths.

Voorhees bags were used in 19 cases. The indications and the influence of bag treatment upon prognosis for mother and child we shall defer until we have discussed the prognosis in general.

Length of Labor.—Our first study was upon the length of labor. We found that in primiparae the average duration of the first stage in dry labor was twelve and one-tenth hours, while Williams estimates the average in all first labors as sixteen hours. For multiparae, the average was seven and one-tenth hours, while Williams' average is eleven hours. Apparently, then, the first stage of labor is shortened rather than lengthened by the absence of the membranes. In a rather high proportion of cases, the first stage was very markedly shortened, for 37 per cent of the primiparae and 64 per cent of the multiparae had a first stage of six hours or less. Cases in which pains were delayed for twenty-four hours or more, though we might expect longer labors because of lessened irritability of the uterus, showed an aver-

age of eleven hours in primiparae, with 32 per cent under six hours, and an average of six and five-tenths hours with 63 per cent under six hours in multiparae.

The second stage showed little difference from the usual average; in primiparae it averaged one and eighty-two hundredths hours, in multiparae nine-tenths of an hour.

The pains in the cases of short labor were usually strong and frequent. In 82 per cent of the dry labors pains were recorded as strong and effective, while in 18 per cent they were only fair or even poor in quality.

In 51 of these cases, or 8.4 per cent, labor lasted over twenty-four hours. Slemons, in this clinic in 1915, found 12.4 per cent of 500 consecutive labors lasting over twenty-four hours. Horner, in his study of 500 cases of bradycardia, reported from the Chicago Lying-In Hospital, found 11 per cent of 4521 cases thus prolonged. That is, contrary to the general opinion; not only is the average duration of labor in these cases with premature rupture of the membranes considerably less than usual, but also the proportion of cases showing prolonged labor is decreased. Moreover, in a high proportion of the cases of prolonged labor, we found one or more additional factors which might have contributed to the prolongation; thus 39 of these cases were in primiparae and of these, 6 were over thirty years of age; 21 had abnormal presentations; of these, 1 was a transverse presentation, 8 were breech, and 12 were occipitoposteriors. Four had contracted pelvises and 7 had babies weighing over 4000 gm.

Operative Interventions.—Notwithstanding the relative shortness of the dry labors, we found that an operative termination was necessary in a rather high percentage of cases. There were 43 breech extractions, or 7.1 per cent; in the total 6500 cases there were 2 per cent. There were 49 deliveries by low forceps, or 8.1 per cent, while the total series showed 5.8 per cent. Since the breech extractions would have been necessary regardless of the premature ruptures, and lifting the head over the perineum with low forceps may be regarded as a potentially normal delivery, we shall concern ourselves more particularly with the other operative procedures.

Of these, we found 25 midforceps, or 4.1 per cent; 9 high forceps, or 1.4 per cent, 1 pubiotomy and high forceps, 2 versions and extractions, 2 unsuccessful attempts at high forceps, the one delivered by craniotomy, the other by Porro cesarean section. One neglected transverse presentation was delivered by decapitation and brachiotomy. That is, 40, or 6.6 per cent, of the cases developed dystocia, requiring serious operative intervention. When we analyze these cases, however, we find, as we did with prolonged labor, a high percentage of additional factors commonly recognized as causative factors in dys-

tocia. Thus 24, or 60 per cent, showed abnormal presentations, of which there were 20 occipitoposteriors, 3 transverse and 1 face presentation. In addition there were 6 contracted pelves, 4 associated with posterior positions, and 3 overlarge babies, 2 in occipitoposterior positions. In other words, more than two-thirds of the cases requiring operative intervention for dystocia showed one or more causes for dystocia aside from the dry labor.

In addition to the operative terminations, we find a number of other operative procedures. The completion of the dilatation of the cervix with the hands, which we might believe necessary frequently, due to loss of the dilating action of the membranes, was used only four times, about half as frequently as in the total series. Cervical lacerations of sufficient severity to necessitate immediate suture were not recorded, hence, apparently, lack of the membranes does not predispose to deep laceration. This confirms a similar observation of Wijssenbeek. Manual rotation of the head in an occipitoposterior position, followed by spontaneous delivery was done in one case. The placenta was removed manually four times. One third degree tear occurred which was repaired.

Since this study was concerned primarily with the influence of premature rupture on the course of labor and its prognosis, we have not included in the series the cases of cesarean section performed for compelling and predetermined indications in spite of the early rupture. Of these, there were 12 during this period of time, with a maternal mortality of 2, or 16 per cent, and no fetal mortality. All except one, a Porro operation, were classic cesareans, so the series confirms the prevailing opinion of the danger of the classic operation after the rupture of the membranes. At the present time, a cervical cesarean would be performed when necessary under these circumstances.

Maternal Mortality.—There was no maternal mortality in the series of 604 dry labors.

Fetal Mortality.—The fetal mortality was 30 cases, or 5 per cent, including stillbirths and deaths in the first two weeks after birth. We have considered viable children weighing over 1500 gm., the standard taken by Williams in his study of fetal deaths in a series of 10,000 cases in Johns Hopkins Hospital. As the mortality in Williams' series was 7 per cent, and that in a similar series reported by Holt from Sloane Maternity was 7.2 per cent, it is apparent that the danger to the child is not increased by dry labor. Nineteen of the cases were still-born; 11 died in the first two weeks of life. The mortality at birth and in the first twelve hours was 23, or 3.8 per cent, practically the same as McQuarrie's mortality of 3.6 per cent in a comparable period in the first 2700 cases in our clinic.

One child was anencephalic. Two macerated children showed anatomic lesions of syphilis and a luetic placenta. A third macerated

child was not autopsied, but the placenta was not luetic. The membranes had been ruptured for a week, and there was intrapartum fever, hence death was probably due to an ascending infection. In 2 cases, death was due to hemorrhage, once from a premature separation of the placenta, once from rupture of a velamentous cord vessel. In 2 cases death was due to prolapse of the cord, a mortality of 40 per cent in the 5 prolapsed cord cases. This is practically the same mortality rate as found in the prolapsed cord cases in the 6500 patients (38 per cent), although the incidence of this complication was twice as high in the dry labors. Three premature children died within a short time after birth. One child of a most uncleanly mother developed bullous impetigo and died on the ninth day after birth. In 15 cases, or 50 per cent, there was definite birth trauma—difficult breech extractions, forceps, or other operative deliveries. One of these was a very long but spontaneous delivery in an elderly primipara. In 3 of the cases no cause for death was evident, in 2 of these even after postmortem examination of the child.

Inflammatory reactions in the cord were noted in 6, or 31 per cent, of the 19 fatal cases in which microscopic examinations of the cord were made. Hence, an ascending infection through the cord vessels must be considered as a cause of death in all of these cases. Yet since 4 of these were operative deliveries, 1 was a markedly prolonged spontaneous labor and the other a premature, it is difficult to weigh fairly the various factors. In one patient with neglected transverse presentation who entered the hospital with a temperature of 38.3° C. after two days labor, the fetus was dead before operative delivery was attempted, and the death may fairly be ascribed to infection. In another, a child in fairly good condition at birth, after a midforceps operation undertaken for maternal exhaustion in a prolonged labor, died on the fourth day with a temperature of 40° C. The prolonged spontaneous labor was afebrile, the patient was not examined vaginally, and the postmortem examination of the child was negative. In the other fatal cases with cord inflammations, it seems impossible to decide between infection and the traumatic factors or prematurity.

As in the prolonged labors and the dystocias, we found so many additional abnormal conditions which might have helped account for them, it is interesting to analyze the cases of fetal death from this standpoint. Here also we find 17 abnormal presentations, or 57 per cent of the fetal deaths; 10 were occipitoposterior, 5 breech, and 2 transverse. Six, or 20 per cent, had contracted pelvis. In 20 cases, or 66 per cent, operative delivery had been necessary.

By way of contrast, we find that in 409 dry labors in occipitoanterior positions in normal pelvis, where the fetus weighed over 2500 gm. the fetal mortality was only 1.2 per cent. This confirms the conclusions of Brodhead, drawn from a singularly uncomplicated series of 182

private cases of dry labor that, in the absence of abnormal conditions, such as contracted pelvis, large child, malpresentations, etc., premature rupture of the membranes is not attended by harmful results for either mother or child.

Maternal Morbidity.—Although there were no maternal deaths in the dry labor cases, we found that maternal morbidity was somewhat greater than the normal. In the total series of 6500 patients, 13.5 per cent had febrile puerperia, including all patients who had a fever over 38° C. even once. Eliminating the cases in which fever was clearly due to mastitis, respiratory infections, etc., the corrected morbidity was 12.8 per cent. In dry labors, the total morbidity was 17 per cent. The corrected morbidity was 15.9 per cent. For the nonoperative cases it was 14.4 per cent, for the operative ones, 22 per cent. Bag labors showed practically the same morbidity as other operative cases; namely, 21 per cent. The morbidity in all cases where the membranes had been ruptured over twenty-four hours was 17.8 per cent. In the cases in which labor was prolonged over twenty-four hours, the morbidity was extremely high—37.2 per cent. Uterine cultures were made as a routine in febrile cases and showed organisms in practically all cases except where the fever was clearly due to an extrapelvic cause.

Fever (38° C. or more) during labor was noted in 15 cases, probably less than the actual incidence, since the temperature during labor was not always recorded. Five of these patients delivered spontaneously; 10 required operative deliveries. In 6 of these patients the puerperium was febrile also. Four patients showed inflammation of the cord; of these, 2 children died and 2 lived. Two children showing no cord inflammation died also, probably from birth trauma.

Omphalitis.—Since Slemons has emphasized the danger to the child from placental bacteremia and Creadick and later Siddall have shown that the inflammatory lesions in the cord formerly ascribed to syphilis are actually due to an ascending bacterial infection from the amniotic cavity, it is interesting to see in what proportion of dry labors we find evidence of such ascending infection. In the earlier cases, microscopic studies of the cord were not made. In 408 of our 604 cases, we find 21 showing a definite omphalitis. This is over twice the percentage found in our own total series and also by Creadick, though much less than that found by Siddall. Sixty-six per cent of the omphalitis cases had had operative deliveries, and in 66 per cent the membranes were ruptured over twenty-four hours before delivery. In five cases, or 23 per cent, the labor itself was over twenty-four hours in length. Of the spontaneous deliveries there was only one in which labor was completed within twenty-four hours of the rupture. A normal spontaneous delivery in dry labor, therefore, seems to carry very little risk of ascending infection, but it is only when labor is prolonged or

the necessity of operative intervention requires invasion of the amniotic cavity that the risk is great. Only 4 of the mothers showed an intrapartum temperature over 38° C. though 15 were over 37.5° C. The puerperal morbidity was 6, or 28 per cent. The fetal mortality was likewise 6, or 28 per cent, but in several of these cases it seemed impossible to decide whether infection or trauma was the most important factor, as is found in our earlier discussion of fetal death in dry labor.

Complicated Dry Labors.—Since uncomplicated dry labors give so little difficulty, whereas contracted pelves, breech deliveries, occipitoposteriors and other complicating factors add so much to the danger in dry labors, the question arises whether the reverse holds true and how much premature rupture of the membranes adds to the danger in these abnormal labors. In breech labors, we find a high proportion, 18.6 per cent, prolonged over twenty-four hours. The fetal mortality was 11.6 per cent, slightly higher than the usual mortality. The maternal morbidity was 16.3 per cent, higher than that in spontaneous dry labors but less than in other operative cases.

The 3 transverse presentations are too few to draw conclusions, but in 2 the children were stillborn, in 1 the labor was over twenty-four hours, and in this one both labor and puerperium were febrile.

Fourteen per cent of the patients with occipitoposterior presentations had labors lasting over twenty-four hours; 36 per cent required operative deliveries, and the fetal mortality was 11 per cent, while the operative incidence in Bell's 510 cases from this clinic was 38 per cent and the total fetal mortality, 6.7 per cent. The maternal morbidity was 17.4 per cent.

Contracted pelves showed 16 per cent of labors prolonged over twenty-four hours, an operative incidence of 41 per cent (Maxwell found 55 per cent in all contracted pelves). The fetal mortality was 25 per cent, while Maxwell found 9.9 per cent in all. The maternal morbidity was 27 per cent.

In abnormal labor, then, the danger, particularly the danger to the child, is definitely increased by premature rupture of the membranes, and this probably explains the fear in which dry labor in general is held, since it is the cases which cause difficulty which remain in mind, and it is easy to ascribe the difficulty to some such obvious factor as the premature rupture.

Treatment by Voorhees Bags.—Treatment by Voorhees bags remains for discussion. It is recommended by some authorities when pains do not set in within two or three days of rupture, and also in the course of labor when cervical dilatation does not progress normally. Our series of bag cases is small, since bags were rarely used for induction of labor in uncomplicated cases. There were 18 in all, 10 inductions;

4 of these were complicated by abnormal presentations, 5 cases where the bag was used in the course of a labor with poor pains and slow dilatation, and 4 cases where the indication did not depend upon the dry labor (2 premature separations and 2 toxemias). The results as they stand are very poor, 47 per cent operative terminations, 31 per cent fetal mortality, 10 per cent intrapartum fevers, 21 per cent puerperal morbidity. Yet none of the fetal deaths were in uncomplicated cases. Two were markedly premature, one of these a breech, the other a transverse presentation. One overlarge child (5075 gm.) died during a difficult breech extraction. The children of 2 patients entering labor with an unengaged head in R.O.P., one of these in a contracted pelvis, succumbed to operative trauma. In one of the premature separations, the child was dead when the patient was first seen.

Used in the course of a long labor which was not progressing normally, the bag completed cervical dilatation in from two to nine hours in 4 cases. Maternal exhaustion necessitated high forceps in 2, and of these, 1 child succumbed. In 1 other case, the bag excited tetanic contractions and had to be removed. The cervix was dilated manually and a normal delivery followed.

Even in the uncomplicated cases, although the children were all born alive, the maternal morbidity was 33 per cent.

Since in all the patients with membranes ruptured over twenty-four hours before labor started, the fetal mortality was 7.1 per cent, with most of the deaths incident to the usual prematurity of such children, and the maternal morbidity 17.8 per cent, it appears that the results with bag induction are far worse than if the case is allowed to continue without operative intervention. Although the series of bag cases was too small for sweeping conclusions, and the bad results were often due to other causes than the bag, it certainly does not encourage the hope that either fetal mortality or maternal morbidity can be reduced by the use of bags.

CONCLUSIONS

1. Dry labor occurred in approximately 10 per cent of 6500 cases.
2. Predisposing factors are primiparity, overdilatation of the uterus, as by large children or twins, abnormal presentations, and lack of engagement of the head. The determining factor appears to be a lack of tensile strength in the membranes, probably due to a deficient development of the connective tissue layers. Many of the labors are premature, but this is probably a consequence rather than a cause.
3. Labor begins in twenty-four hours or less in 90 per cent of cases; of those delaying longer, two-thirds are premature. The longest delay was nineteen days.

4. Castor oil and quinine were successful in inducing labor in over 90 per cent of the cases in which they were used. No fetal deaths could be attributed to the quinine.

5. The average length of the first stage of labor was considerably shorter than that usually accepted for normal in both multiparae and primiparae. One-third of the primiparae and two-thirds of the multiparae had very short first stages—six hours or less. The second stage was not influenced.

6. Labors prolonged over twenty-four hours were less frequent than reported in unselected series. Dry labors which were prolonged and also the cases of dry labor developing dystocia requiring serious operative interventions, showed other abnormalities, as malpresentations, contracted pelves, overlarge children, etc., in a high percentage of cases.

7. Fetal mortality was not higher than normal and a high percentage of the fetal deaths occurred in uncomplicated cases.

8. There was no maternal mortality in 600 cases. Maternal morbidity was slightly higher than that found in our 6500 unselected cases.

9. Cord inflammations were twice as frequent as found in our 6500 cases, but occurred almost entirely in prolonged labors or in operative cases.

10. In abnormal labors, as those complicated by contracted pelves, malpresentations, etc., the fetal risk is considerably increased by premature rupture of the membranes. The maternal risk as measured by maternal morbidity is also increased slightly. This may explain the bad repute of dry labor in general, since it is the cases which cause difficulty which remain in mind, and it is easy to ascribe the difficult to some such obvious factor as the premature rupture.

11. Results with bag treatment were very poor, and, although the series was small and the bad results often due to other causes than the bag, offer little hope of reduction either of fetal mortality or maternal morbidity.

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A REVIEW OF THE PATHOLOGY OF ONE HUNDRED FOUR
CONSECUTIVE MISCARRIAGES IN PRIVATE
OBSTETRIC PRACTICE*

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IN APRIL, 1922, I reported before the Obstetrical Section of the New York State Medical Society 39 consecutive abortions in which the products of conception had been carefully studied. Since then my series has increased to 104 consecutive intrauterine pregnancies which terminated or were interrupted before the period of viability. All of these, with one exception, have been examined by Dr. George L. Streeter of the Carnegie Institute of Baltimore and through his kindness and help it has been possible to make the following report.

Eighty-five were inevitable abortions in that the tissues were dead before the uterus was emptied.

Let us first dispose of the other 19 abortions in which the products of conception were living at the time of the termination of pregnancy. Ten of these were artificially terminated as follows: 2 came into my office after criminal methods had been employed; 6 were therapeutic abortions; and in the remaining 2 the uterus was emptied because of hemorrhage due to placenta previa. Of the 9 remaining in this group, 2 abortions immediately followed trauma sufficiently violent to rupture the amniotic sac; 1 was immediately after appendectomy with drainage. These last 3 patients have all been pregnant two or three times since the above events, have had no abortions, and the children have been healthy and strong.

The remaining 6 will have to be taken up separately.

Patient No. 1593. This patient has a history of 2 previous abortions at four months and two and a half months respectively. Further details of these are lacking. Both parents of the patient had syphilis but repeated tests of the patient's blood have all been negative. The patient has a history of definite pelvic infection and has had two severe attacks of salpingitis, one before and one a few months after this abortion which was at eighteen and a half weeks and spontaneous. Streeter wrote after studying the products of conception: "From an examination of the placenta it is my impression that the growth of the villi is not as luxuriant as is usually found in fetuses of this size, but the villi are normal and show none of the changes we usually associate with syphilis."

Three patients were responsible for the remaining 5 abortions in this group and all of these seem to fall into one class.

The first patient, No. 1288, aborted at twenty weeks. The report from Dr. Streeter was: "A male fetus and placenta, both of which appear normal, so

*Read at a meeting of the New York Obstetrical Society, May 8, 1928.

that we may be sure that development was in progress a very short time before the miscarriage." The history leading up to this is as follows: Her first pregnancy, when twenty-six years of age, terminated with toxemia, manual dilatation and delivery at seven months of a 2 pound 6 ounce baby which lived two days. The following year she had an abortion at four months. Again a year or so later she had an abortion at three months and the following year an abortion at five months. The patient was badly torn at her first delivery and was repaired in 1918. The patient was two months along in her fifth pregnancy when I first saw her. She had a very slight showing about the time she skipped her first period. There was no sign of toxemia. She was kept very quiet in bed, gradually allowed to walk around the room and after five months was walking up the stairs once a day. She began to have indefinite pain September 30, 1920, and was sent at once to the hospital. After twenty-four hours she suddenly started in active labor and delivered herself of a 5 pound 6 ounce female child, estimated to be about four weeks premature. The baby did perfectly and is alive and well today. The patient started her next pregnancy October 21, 1921. She was kept very quiet as before. In spite of this the patient started in labor on May 13 and delivered herself of a very small male baby that lived but thirty minutes, estimated to be eleven weeks premature. With the present pregnancy which ended in abortion, the patient was kept practically in bed. She had two slight attacks of bleeding after straining at stool. The membranes ruptured while the patient was lying quietly in bed and she aborted spontaneously shortly afterwards.

Thus we have here a patient who, following toxemia in her first pregnancy, has had six pregnancies terminate before term, and in only one case was a child capable of surviving obtained. This patient had a negative Wassermann, and physical examination in 1925 failed to show any apparent cause for these abortions. Her blood pressure always was low and she never showed anything abnormal in the urinalyses.

The second patient, No. 1301, had an abortion at seventeen weeks in May, 1920, and again at eighteen weeks in November, 1920. Both of these were reported as living up to the time the uterus was emptied and were considered absolutely normal by Streeter. The past history of this patient was as follows: With her first pregnancy seven years before her first abortion she had toxemia. The uterus was emptied at seven months and the baby did not live. Shortly after this the patient developed a condition closely resembling epilepsy, supposed to be due to intestinal toxemia. To ameliorate this condition the appendix and ascending colon were removed some three years before her second pregnancy. This began December 28, 1919, and I saw her first in April, 1920. Except for slight bleeding on March 23, the pregnancy had been proceeding normally. On April 30, she ran a few steps to catch a train, shortly afterward had a gush of fluid and aborted the next day. As I say, Streeter reported normal living tissue at the time of abortion. Her third pregnancy began July 1, 1920. The patient was kept very quiet and on luminal to prevent any epileptiform attacks. On the twelfth of November the patient was very apprehensive, feeling that an attack was coming on. She was sent to the hospital and given chloral. She had several attacks of twitching that day, a bloody discharge was noted that night and she aborted the next day. Streeter again found all normal. The patient had a complete physical examination at this time. The Wassermann was negative and no renal condition could be found to account for the abortion. The next pregnancy began March 2, 1922. The patient was kept in bed and given opium suppositories

whenever she felt any sensation of pelvic congestion. Toward the end of pregnancy the patient had a slightly elevated blood pressure, once as high as 136. The urine occasionally showed the slightest possible trace of albumin, no blood or casts. The patient ruptured her membranes when within two weeks of term and had a 6 pound 2 ounce male infant, which has done perfectly well since birth. The next pregnancy started September 4, 1923. She was kept in bed during the first seven and one-half months, then given more and more freedom the last six weeks. The patient went to term and delivered normally a seven and a half pound male baby which has done perfectly well since. She showed no symptoms of toxemia at all with this last pregnancy. That adhesions in the pelvis from the previous laparotomy may have caused these two abortions has to be entertained as a possibility.

The third patient was a primipara, eighteen years old. The pregnancy was proceeding normally when the patient, then about twenty-one weeks pregnant, fell from a sleigh into a snow drift, shortly afterward began to have a discharge and aborted spontaneously. The fetus was alive at the time it was born but was not examined by Dr. Streeter. Her next pregnancy began June 1, 1921. The patient was urged to keep moderately quiet but was not kept in bed. On November 8 she began to have a bloody discharge and aborted the next day. The products of conception were sent to Dr. Streeter, who reported normal living tissue up to the time of abortion. Complete examination, including Wassermann, failed to show anything abnormal. Since these events I have learned that this patient has had two more pregnancies, has remained practically in bed during each pregnancy and has two living healthy children.

So much for the 17 patients, 19 of whose pregnancies ended before the period of viability with normal living tissues at the time of abortion. In none of these cases was there any history or evidence of endometritis and in none of these cases was there any uterine displacement.

We come now to the 85 pregnancies in which development had ceased before the expulsion of the products of conception, and all in or before the twentieth week.

In 3 of these abortions the tissues were normal and little or no maceration had taken place but development had ceased days or weeks before expulsion. The first one was in a patient with multiple fibroids who had been bleeding every day for many weeks. A hysterectomy was done and a fetus was found in utero. Streeter reported maceration in the cord and the placenta; he estimated the development as twenty weeks and that fetal death had taken place four weeks before the hysterectomy. Here apparently the etiologic factor was the fibroid growth of the uterus. Pierson¹ studied a series of 191 patients at the Sloane Hospital which showed, clinically important, fibromyomas. He found that spontaneous abortion or premature labor occurred in 24.1 per cent of these.

The second in this series of three abortions is as follows:

It was her sixth pregnancy. There was nothing remarkable in the history of her first three and the children are living and well. The fourth ended in an operation for central placenta previa, sixty-nine days before term. The baby

lived but ten hours. The fifth pregnancy ended in an abortion at eleven weeks. Streeter reported an ovum of four weeks' development and a diagnosis of defective germ plasm. Following this the patient was curetted by a leading gynecologist and the cervix repaired. "Curettings showed a mild polypoid gland hypertrophy." The patient had increasing anemia before and after this operation and had a sharp attack of pyelitis. She was in very poor physical condition when the sixth pregnancy began, January 22, 1923. Dr. George Minot was taking care of the patient, trying to improve her blood condition. On June 2, without any trauma or undue exertion, the patient noticed a slight watery discharge from the vagina. Later in the day this became blood tinged. The next day the patient began to have considerable discomfort and on June 4 after two or three cramp-like pains, presented an intact bag of membranes at the vulva. The uterus was emptied with only very moderate bleeding, but the patient continued to ooze until packed. Later in the day the patient was transfused because of profound anemia. The products of conception in this case are described by Dr. Streeter as follows: "A female fetus, normal in form and shows no evidence of maceration. From its weight and measurements it has a development of a little over eighteen weeks, whereas the menstrual age is twenty-two weeks. I think we must conclude that the fetus was dead three or four weeks before the expulsion occurred. The placenta on section shows no abnormality other than slight maceration. I imagine the clinical history of anemia and other functional disturbance produced this effect on the ovary rather than on the embryo after development had been inaugurated." The patient has had one pregnancy since, in 1925, which again terminated in central placenta previa five weeks before term. The baby weighed five pounds and has done perfectly well.

The third patient in this series, after one and one-half years of sterility, had a dilatation and curettage. The curettings showed "polypoid and hypertrophied endometrium." The patient had one period following the operation and immediately became pregnant. She had long continued and at times fairly profuse bleeding during the second and third months of pregnancy but with rest in bed the pregnancy continued and a full-term nine pound male child was easily delivered by low forceps. The child is well and strong today. Following this pregnancy, after two years and three months, the patient again had a dilatation and curettage, the curettings this time proving normal. At this time a laparotomy was performed and the right ovary, being completely replaced by multiple follicular cysts, was removed and the uterus was suspended by the round ligaments. After this operation, over a year elapsed before another pregnancy occurred. Because of previous bleeding the patient was kept very quiet during the early months, but in spite of these precautions the patient began to have a slight bloody discharge when about four months pregnant and ten days later aborted. Dr. Streeter reports as follows: "Male fetus, normal, eighteen weeks development, has been dead for two weeks." He suggested that this abortion might be due to a faulty hormone reaction. It is interesting to note in this connection that the fetus was a male, in view of the work of Oscar Riddle² at Cold Spring Harbor. The patient and her husband were thoroughly examined following this miscarriage and nothing abnormal found in either, except that the patient herself had a blood pressure of 85/45 and a basal metabolism of -5. She was therefore put on small doses of thyroid, $\frac{1}{2}$ gr. t.i.d. After four normal monthly periods the patient became pregnant. During pregnancy the doses of thyroid extract were gradually increased so that she was getting two and one-half grains daily the last few weeks. The patient was kept moderately quiet the early months of pregnancy because of her history. Everything was perfectly normal, however, and on the twenty-ninth of

last March she delivered herself normally of a 7½ pound female infant. The child is perfectly healthy and growing most satisfactorily.

It does not seem as if endometritis or uterine displacement could have played any rôle in these abortions.

This brings us to the 82 abortions remaining, all considered due to defective germ plasm.

What is defective germ plasm?

Vignes,³ has written a long theoretical discussion of the causes of abortion. He considers the possibility of irregular menstruations being very early abortions, that is, where the period is delayed two days to over a week. He also considers the possibility if not the probability of complete resorption of these early defective embryos in man. He goes on to say that every egg is not capable of fertilization and so of course every abortion is not pathologic. There is variation in fertility among the different races and it is possible that some individuals may be biologically incompatible.

Streeter⁴ thus describes "defective germ plasm": "It must be understood that the term is used on the basis of behavior rather than on microscopic appearance. The defective egg is one that does not develop properly. If one had a defective egg alongside of a virile egg it is not likely that they would present any particular differences in appearance. It is the way they react in the mechanism of development that distinguishes the two. * * * One is prepared to make the diagnosis of defective germ plasm on the basis of failure in development rather than in any characteristic histologic differences in tissue."

Rock⁵ states that most spontaneous abortions in human beings are due to intrinsic disturbance in the fertilized ovum or in the maternal organism and not to the traditional extrinsic environmental accidents to the mother. He further considers that the causes of sterility and abortion are probably in large part identical, the two conditions being but different degrees of diminished fertility.

Macomber⁶ discusses fully the etiologic importance of defective germ plasm and finds that his sterility patients give a history of twice as many abortions as have the average patients.

Williams⁷ in the 1926 edition of his textbook states that "one of the most usual causes of death of the fetus is to be found in the abnormalities of development which are inconsistent with life."

So much for the literature; sufficient to state that few authors refer to the rôle of defective germ plasm in abortion, and practically none emphasize the importance of routine examination of the products of conception. And, yet, we have 82 abortions out of 104 where the unqualified diagnosis was defective germ plasm.

Let us take up the 82 abortions where this diagnosis was made by Dr. Streeter and see if we can learn anything from a close analysis.

In 8 of these abortions the patients were primiparae. There is no history of subsequent pregnancy. One at least of these patients had been under treatment for sterility for several years. Two of these patients showed retroversion of the uterus and a third had endometritis.

Let us now turn to the chart.

TABLE I

PATIENTS	ABORTIONS	REPORTED D. G. P.	LIVING NORMAL CHILDREN	DEAD CHILDREN OR STILLBIRTHS	RETRODISPLACE- MENTS OF UTERUS OR ENDOMETRITIS
33	33	33	I 68 (2.06)	5	7
28	68	41	II 52 (1.86)	9	7
28	2	0	III 75 (2.68)	4	13

The next 33 abortions occurred in multiparae who have had only one abortion each, and that one studied by Streeter. As far as fertility is concerned we find that these 33 patients have had 68 living, healthy, normal children and 5 stillbirths or children who have died shortly after birth. This would give 2.06 living children per patient. It is interesting to note that only 7 of these 33 patients showed evidence of either endometritis or uterine displacements.

Twenty-eight patients were responsible for the 41 remaining abortions. Each gave a history of 2 or more abortions, 68 abortions in all. In my previous paper⁸ I reported an incidence of miscarriage of about 1 in 10 pregnancies. I have found that practically the same ratio exists in this larger series. So if 1 pregnancy in every 10 ends in abortion it is obvious that these 28 patients have had more abortions than they were entitled to and in so far must be regarded as pathologic.

In comparing the series of multiparae who have had only one abortion with these, we find that the former series is distinctly more fertile, 2.06 living children as compared with 1.88 in the latter series. As a checkup I took the last 28 multiparae I had delivered, not in this series, and I found that the number of living children was 2.66. It is also interesting to note how the stillbirths and neonatal mortality varied in these groups, 5 in the first group, 9 in the second, and 4 in the third. Obviously the number of cases is far too small to allow of any such inference being drawn, but it certainly suggests a tendency to more virile germ plasma in the latter group where abortions were practically absent. Also it can be seen that there seems to be no connection between uterine displacements and abortions in these series, for in the group with 68 abortions only 7 out of 28 patients gave evidence of uterine displacement or endometritis while in the group with 33 abortions, 7 out of the 33 gave such evidence and in the group with only 2 abortions, 13 of the 28 women had uterine displacements and several of these had slight endometritis as well.

Now to return to this interesting group of 28 patients who have had 2 or more abortions each, I am taking only the 10 cases that have had careful study of the products of conception. Several of the other 18 cases in this series might prove equally or more interesting, but as I have had the opportunity of seeing the products of only one of the

TABLE II

PATIENT'S NO.	AGE AT 1ST CONCEPTION	ABORTIONS	LIVING CHILDREN	DEAD OR STILL- BORN	PELVIC LESION	HEALTH		? OF RESORPTION
						HUSBAND	PATIENT	
555	26	2	3	0	Retroversion	Not examined	Excellent	0
1863	26	3	1	0	Retroversion	Perfect	Hypothyroidism; B.M. -17	X
873	28	2	4	0	0	Not strong	Normal	0
1541	31	2	1	0	Multiple fibroids, Op. 1925	Perfect	Hypothyroidism	X
1352	23	2	1	1	0	Obese	Normal	X
1124	24	3	4	0	Endocervicitis	Focal infection	Focal infection; B.M. -21	X
1229	28	2	0	1	0	Not examined	Normal	0
1318	25	3	1	1	0	Obese and has hy- pertension	Normal	0
1383	26	3	2	1	0	Lowered resistance for years. Py- elitis, ill 3 mo. 1926	Normal; B.M. +5	0

abortions per patient and sending that to Dr. Streeter for examination I feel we had better select for more careful study these other 10 where the story is more fully known.

The first of these 10 is a patient who has chronic nephritis, and has had four abortions. The first and fourth only were in our care and studied by Dr. Streeter but the other two were apparently similar from the story. They were all spontaneous and showed fibrous degeneration of the decidua and were retained for several weeks after development had ceased.

Of the remaining 9 patients 5 had 1 pregnancy each before coming to me for care. The other 4 have been patients of mine since the beginning of their obstetric history.

All these patients at the time of the first abortion were over twenty-four and under thirty-two years of age. Four of these patients have had 3 abortions and the others 2 each. Dr. Streeter has of course examined all of these, compared the products of conception with the previous slides and, I again emphasize, in every case his decision has been defective germ plasm. Most if not all of these showed marked hydatiform degeneration of the villi as well as maceration. All of these patients save one have had at least one living child and I know that in that case definite precautions have been taken to prevent the possibility of conception.

While I know that it is most important, as a matter of fact it is a very difficult thing in private practice to insist on complete physical examination of husband and wife after an abortion. In spite of this most of these husbands have had physical examinations and several of the 9 were found to be below standard. Two were obese and two are seldom really strong. One has had several teeth removed because of focal infection since the date of his wife's last abortion. Several work altogether too hard, their habits are none too good and it is within the realms of possibility that some of them may be responsible for the defective germ plasm. Two husbands only have been examined thoroughly and both of these had perfectly normal active spermatozoa in ample quantities.

Four of the above mothers have had their basal metabolisms studied. In 3 it was negative. One of these patients with negative basal metabolism and a history of 2 abortions was put on thyroid extract, about 5 to 10 grains daily. While taking thyroid she became pregnant, went successfully to term and now has a splendid healthy infant. Two and a half years previously she had a laparotomy improving a slightly retrocessed uterus and several small fibroids were removed. No pregnancy took place, however, until she started taking thyroid extract.

Five of these patients have never had any evidence of endometritis or uterine displacement. One patient has had endocervicitis but this

has existed since her first pregnancy and she has had three children in spite of this condition. Since then she has had 3 abortions and now is found to have a basal metabolism of -21. Both she and her husband have had several teeth removed because of focal infection.

One patient has often had a retroverted uterus, in spite of which she has had three children as well as these two abortions. The remaining patient had at times a retroverted uterus. Following her first abortion, she was operated upon; her retroverted uterus was suspended and a cystic ovary resected. She became pregnant shortly after this operation, went successfully through her pregnancy and has a healthy child a year and a half old. Following this her uterus was found held in perfect position, but she became pregnant a year later and again miscarried. She was then found to have a basal metabolism of -17 and definite symptoms of hypothyroidism. She has been on thyroid extract for several weeks now and feels very much better.

This last patient and three other patients in this series have had once or twice delayed periods and definite symptoms of early pregnancy. The uterus in each case seemed distinctly enlarged. Then the patient has had a slight flow for a few days and examination after the flowing had ceased showed a perfectly normal uterus. This has happened occasionally with patients in the other groups and certainly leads me to the suspicion that these may have been cases where the products of conception were entirely resorbed. These cases have been under such close observation that it does not seem possible that an embryo even of minute size could have escaped unnoticed.

So much for an analysis of 104 consecutive abortions.

As a basis for a statistical paper this is a small number, but nevertheless it is sufficiently large to yield certain conclusions, which I will now briefly summarize.

In the first place I think it is fair to say that as a result of this study we cannot but feel that endometritis and retroversion play a very minor rôle in the etiology of abortions.

Second, defective germ plasm is the chief cause of abortion.

Third, trauma when sufficiently violent to rupture the amniotic sac is an undoubted cause of abortion.

Fourth, multiple fibroids may cause the death of the fetus in utero with subsequent abortion.

Finally, I believe that defective germ plasm may exist normally and account for an occasional abortion in perfectly healthy individuals with unimpaired fertility; but that it is much more likely to occur where the patient is over- or undernourished or poisoned from within or without. And here besides focal infection we should consider the effect of faulty endocrine function, especially deficient thyroid secretion, defective development of the corpus luteum, and anterior lobe

hormones. It is also possible that focal infection, faulty endocrines, fatigue or other poisons may play a rôle in the creation of spermatozoa capable of impregnating the ovum but lacking the vitality to bring the egg to full development.

Fellow obstetricians, I beg of you to take this subject seriously to heart. We read stirring pleas for the necessity of postmortem examinations in the field of general medicine but scarcely a word from the obstetricians for the study of products of conception following abortion. To obtain permission for an autopsy requires time and eloquence. Products of conception in these early abortions are the unquestioned property of the operator. I believe that the obstetrician who, after an abortion, throws away or fails to have examined by an expert the products of conception and then informs the disappointed patient that she has done too much automobiling, is guilty of negligence, and is through ignorance or laziness giving an explanation as cruel as it is false.

If we are ever to know anything about pathologic embryology it can be only by the combined efforts of clinicians working with laboratory experts. The necessity of studying the products of conception must be taught in our medical schools and the truth about abortion given to the general public.

Then and then only can we build up an accurate method for treatment of threatened abortion, so that should the pregnancy fail, proper steps can be taken to ensure success in the future.

I wish to express my indebtedness to my colleagues, Drs. W. T. Sherman Thorn-dike and Benjamin Tenney for their cooperation and help in the preparation of this paper.

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24 MARLBOROUGH STREET.

(For discussion, see page 121.)

THE DECIDUAL REACTION IN EXTRAUTERINE PREGNANCY*

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IN A STUDY of 74 cases of extrauterine pregnancy, evidence was found for the belief (1) that a decidual reaction of greater or less extent occurs constantly at the site of implantation; (2) that the decidual tissue persists as long as the chorionic villi are intact; (3) that following the termination of the pregnancy by hemorrhage with resultant degeneration of the chorionic villi, the local decidual tissue undergoes involution, and (4) that a distant decidual reaction in other portions of the tube, uterus, or elsewhere is not constant and that when it does occur, it may persist after the degeneration of the chorionic villi and the complete involution of the local decidual tissue.

Concerning the relatively frequent occurrence of vaginal bleeding in extrauterine pregnancy, the impression is gained from a study of 17 curettings in the series that it probably depends upon changes other than the casting off of uterine decidual tissue. In fact the bleeding was much greater in the cases in which no decidual tissue was present in the curettings.

That there is still considerable uncertainty concerning the decidual reaction in extrauterine pregnancy is indicated by the following statement of Williams:¹

"Bland Sutton in 1891, and Füh and Griffiths a few years later, pointed out that the decidual reaction in the tube was nothing like so extensive as was generally believed; while Kühne, Asehoff, and Kreisch were skeptical of its existence, and contended that the cells, which had formerly been described as decidual, were really of fetal origin. The first mentioned view has been confirmed, by subsequent observers, and at present no one claims that a continuous decidual membrane is formed.

"On the other hand, it is erroneous to contend that a decidual reaction is always lacking, as it is possible by careful study to distinguish decidual cells, and to differentiate clearly between them and fetal cells. The former are usually found in discrete patches in the tips of some of the folds of the mucosa in the neighborhood of the ovum. Furthermore, one can occasionally find decidual cells scattered between the fetal tissues at the placental side, but I have never observed a decidual membrane analogous to the decidua vera or serotina in uterine pregnancy.

"That the authors who deny the existence of decidual cells in the tube take too extreme a view is shown by the fact that they have been repeatedly observed by Webster, Both, Couvelaire, Kermauner, Young, myself and others. Moreover, the possibility of a decidual reaction is demonstrated by the fact that I have repeatedly observed characteristic decidual cells in the nonpregnant tube. Observations of this character are beyond criticism, as in such cases it is impossible to confuse

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decidual with fetal cells. Furthermore, Mandl, Lange, and I have noted an identical reaction in the tubes in certain cases of uterine pregnancy.

"The absence, or comparative scantiness, of the decidual reaction is of interest not only from a scientific point of view, but also has a distinctly practical bearing, as it would seem to offer a satisfactory explanation for the invasion and destruction

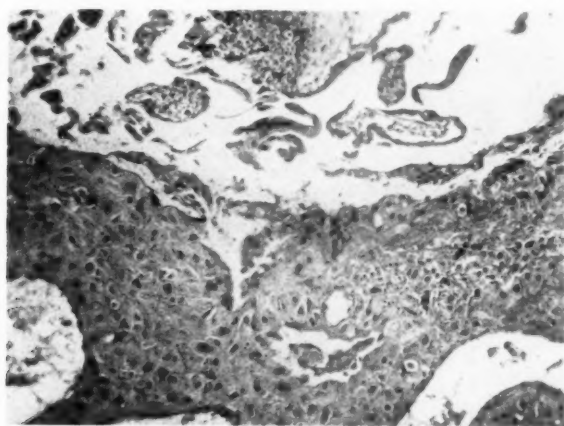


Fig. 1.—(Mag. 100x.) Tubal Pregnancy. Chorionic villi intact, decidual tissue intact.

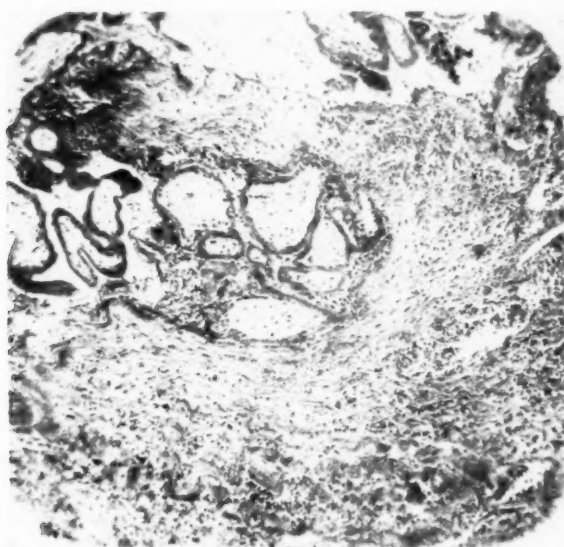


Fig. 2.—(Mag. 100x.) Tubal Pregnancy. Chorionic villi degenerated, no intact decidual tissue.

of the tube wall by the fetal elements. In uterine pregnancy, such an invasion is noted only in the rare instances in which there is an imperfect development of the decidua, and it would therefore appear that one of the main purposes of its formation is to protect the maternal tissues against the invasion and corrosive action of the fetal cells."

Polak and Wolfe² from their observations conclude:

"a. Majority of tubal pregnancies are incomplete tubal abortions which are not completely terminated at the time bleeding occurs; and that vaginal bleeding persists as long as the ovum is alive and partially attached to its tubal bed.

"b. That many cases are operated before the ovum dies. In these, decidual reaction is found in tube and uterus.

"c. In those operated after death of the ovum, no decidual reaction is found."

Our study of the decidual reaction in 74 cases of extrauterine pregnancy is summarized in the following tables:

TABLE I.—CASES FROM MOUNT SINAI HOSPITAL

DATE OF OPERATION	SERIAL NUMBER BY DR. BUBS	LABORATORY NUMBER	AGE	PORTION OF TUBE IN- VOLVED			ALL OR MAJORITY OF CHORIONIC VILLI INTACT	ABOUT HALF OF VILLI INTACT	ALL OR MAJORITY OF VILLI SHOW ING DEGENERA- TIVE CHANGES	DECIDUAL REACTION					
				PROXIMAL	MID	DISTAL				TUBE		UTERUS	OVARY		
										LOCAL	DISTANT		DISTANT	LOCAL	DISTANT
7/16/23	45	8412	29	+	+	+				0	0	N.S.		0	
9/ 2/23	46	8662	30	+				+		+	0	N.S.		N.S.	
9/19/23	47	8716	40			+				+	0	+		N.S.	
12/ 2/23	48	8906	26			+	+			+	0	N.S.		N.S.	
12/ 5/23	49	8916	38			+			+	+	0	0		0	
3/27/24	54	9252	32			+				+	0	N.S.		N.S.	
4/ 7/24	55	9285	28			+	+			+	+	N.S.		+	N.S.
7/ 2/24	57	9507	28		+		+			+	0	0		N.S.	
7/10/24	58	9531	31	+			+			+	0	N.S.		0	
8/11/24	59	9615	30		+				+	0	0	N.S.		0	
11/ 4/24	62	9847	37	+	+					0	0	0		N.S.	
12/10/24	63	9934	31			+			+	0	0	atypical		0	
12/26/24	64	9966	24		+				+	0	0	N.S.		N.S.	
3/21/25	65	10228	31	+					+	0	0	N.S.		N.S.	
4/ 1/25	66	10261	26		+	+			+	0	0	N.S.		N.S.	
4/ 2/25	67	10263	35		+	+	+			+	0	N.S.		N.S.	
6/ 1/25	68	10402	20		+		+			+	0	N.S.		N.S.	
6/ 3/25	69	10416	28	+					+	0	0	N.S.		N.S.	
7/24/25	70	10569	27		+			+		+	0	N.S.		N.S.	
8/19/25	71	10642	37	+				+		+	0	N.S.		+	
8/26/25	72	10631	35	+					+	0	0	0			
9/30/25	73	10778	40		+		+		+	0	0	0		N.S.	
1/ 9/26	74	11086	26	+			+			+	0	N.S.		N.S.	
3/11/26	75	11268	24		+			+		+	0	N.S.		N.S.	
6/16/26	76	11525	21		+	+	+			+	0	0		N.S.	
9/ 2/26	77	11753	39		+			+		+	0	0		N.S.	
9/17/26	79	11809	40	+					+	0	0	+		N.S.	
9/22/26	78	11827		+					+	0	+	0		0	
1/21/27		12188	30			+			+	0	0	N.S.		0	
2/ 7/27		12255	29			+			+	0	0	N.S.		0	
2/19/27		12310	30		+			+		+	0	N.S.		N.S.	
2/22/27		12317	30		+					+	0	N.S.		N.S.	
3/ 4/27		12363	27	+			+			+	0	+		N.S.	
3/ 7/27		12373	30			+			+	0	0	N.S.		0	
3/24/27		12448	29			+			+	0	0	0		0	
8/26/27		12958	31			+			+	0	0	0		N.S.	
10/ 7/27		13115	35	+	+			+		0	0	N.S.		0	
11/ 7/27		13223	45	+					+	+	0	N.S.		N.S.	
12/ 4/27		13314	23	+					+	0	0	N.S.		N.S.	
12/16/27		13347	29	+				+		+	0	N.S.		0	
2/ 7/28		13524	32	+					+	+	0	atypical		0	
2/17/28		13557	22		+				+	0	0	N.S.		0	

TABLE I—CONT'D
WOMAN'S HOSPITAL OF CLEVELAND

DATE OF OPERATION	SERIAL NUMBER BY DR. RUBIN	LABORATORY NUMBER	AGE	PORTION OF TUBE IN- VOLVED			ALL OR MAJORITY OF CHORIONIC VILLI INTACT	ABOUT HALF OF VILLI INTACT	ALL OR MAJORITY OF VILLI SHOW- ING DEGENERA- TIVE CHANGES	DECIDUAL REACTION				
				PROXIMAL	MID	DISTAL				TUBE		UTERUS	OVARY	
										LOCAL	DISTANT		LOCAL	DISTANT
1/21/25		8307	32						+			N.S.	0	
3/31/25		8429	41	+	+	+			+			N.S.	N.S.	
4/ 5/25		8435	28			+				+		N.S.	N.S.	
5/19/25		8497	26	+						0		N.S.	0	
5/21/25		8499	30		+				+	0	0	N.S.	N.S.	
6/ 9/25		8564	30	+					+	+	0	N.S.	0	
11/12/25		8736	35	+				+		+	0	N.S.	N.S.	
12/24/25		8792	38			+		+		+	0	N.S.	0	
3/ 3/26		8933	30		+				+	0		N.S.	0	
4/17/26		8954	43			+			+	0		N.S.	0	
11/ 5/26		9255	33	+	+				+	0	0	N.S.	0	
1/26/27		9367	23			+			+	0	0	N.S.	0	
1/25/27		9368	39		+				+	+	0	N.S.	N.S.	
2/28/27		9429	24		+	+			+	0	0	N.S.	0	
3/29/27		9513	27		+	+			+	0	0	N.S.	0	
7/16/27		9626	19			+			+	0	0	N.S.	0	
7/22/27		9633	23			+			+	0	0	N.S.	0	
8/ 2/27		9643	2	+	+	+			+	0	0	N.S.	0	
9/31/27		9748	40	+			+			+	0	+	0	
2/16/28		9885	27			+			+	0	+	N.S.	0	

HOSPITAL CLINIC OF CLEVELAND

11/21/24		1057	32			+	+		+	+	0	N.S.	+	
1/14/25		1089	28	+					+	+	0	N.S.	N.S.	
2/19/25		1110	31	+					+	+	0	N.S.	N.S.	
5/29/25		1190	33	+	+	+		+		+	0	N.S.	N.S.	
6/16/25		1203	27		+	+			+	0		N.S.	0	
5/12/26		1453	22			+			+	+	0	N.S.		
5/30/26		1465	27		+		+		+	+	0	N.S.	N.S.	
8/23/26		1572	33			+			+	+	0	N.S.	N.S.	
9/22/26		1622	39	+					+	+	0	N.S.	0	
2/15/27		1743	25	+	+	+			+	0	0	+	N.S.	
5/ 9/27		1805	31	+	+				+	0	0	N.S.	N.S.	
2/28/28		2104	35		+	+			+	0	0	N.S.	0	
Total		74		29	31	32	15	11	44	36	3	5	3	0
		Cases												

NS.=No Specimen.

DISCUSSION OF FINDINGS

From the study charted above, the following conclusions have been reached:

About one-half of the patients with tubal pregnancy in this series were operated upon at a time when the majority or all of the chorionic villi and local decidual tissue were still intact. In the other half, the operations were performed at a time when the majority or all of the villi were partially or almost completely degenerated and the local decidual tissue completely or almost completely involuted. In other words, the evidence suggests that a decidual reaction of greater or less extent constantly occurs locally in tubal pregnancy and that following

the termination of the process by hemorrhage with resultant degeneration of the villi, the decidual tissue undergoes involution. (See Figs. 1 and 2.)

The decidual reaction in the uterus in cases of extrauterine pregnancy has been found to be inconstant and behaves as does the distant decidual reaction in other portions of the affected tube and in other sites. For instance, as will be seen from Table III no decidual reaction was observed in the uterus in 5 cases in which this reaction was present in the tube in the neighborhood of intact chorionic villi, and on the other hand was present in 2 cases in which no decidual tissue was present at the implantation site where the chorionic villi showed degenerative changes. (See Figs. 3 and 4.) In this series then, the uterine curettings in one-half of the cases yielded no information or false information concerning a viable tubal pregnancy. The distant decidual reaction in the tube was likewise found inconstant and ap-

TABLE II.—DECIDUAL RELATION IN EXTRAUTERINE PREGNANCY

	FALLOPIAN TUBE					UTERUS				OVARY				
	INTACT DECIDUAL TISSUE LOCALLY	ALMOST INVOLUTED OR NO DECIDUAL TISSUE LOCALLY	INTACT DISTANT DECIDUAL TISSUE	NO DISTANT DECIDUAL TISSUE	NO RECORD DISTANT PORTIONS OF TUBE	INTACT DISTANT DECIDUAL TISSUE	INTACT DISTANT ATYPICAL DECIDUAL TISSUE	NO DISTANT DECIDUAL TISSUE	NO SPECIMEN	INTACT DECIDUAL TISSUE LOCALLY	NO DECIDUAL TISSUE LOCALLY	INTACT DISTANT DECIDUAL TISSUE	NO DISTANT DECIDUAL TISSUE	NO SPECIMEN
TOTAL	36	37	3	51	20	5	2	10	57	3	1	0	32	38
All or majority of chronic villi intact	15		1			2		2		2				
About half of villi intact	9	2						1		1				
All or majority of villi showing degenerative changes	10	34	2			2	2	8			1			
No record of condition of villi	3	2				1		1						

TABLE III.—RELATIONSHIP OF UTERINE AND TUBAL DECIDUAL REACTIONS IN TUBAL PREGNANCY

	UTERINE CURETTINGS		
	INTACT DECIDUAL TISSUE PRESENT	ATYPICAL DECIDUAL TISSUE PRESENT	NO DECIDUAL TISSUE PRESENT
TOTAL	5	2	10
Intact decidual tissue locally in tube	3	1	4
Almost involuted or no decidual tissue locally in tube	2	1	6

parently occurs and involutes much as that in the uterus in tubal pregnancy.

The study of the cases described above supports the view that the usual termination of tubal pregnancy by hemorrhage depends upon the inability of the relatively scant decidua to prevent invasion of the large vessels of the tubal wall by the trophoblast.



Fig. 3.—(Mag. 100x.) Tubal Pregnancy. No intact decidua at implantation site. (Chorionic villi degenerated.)

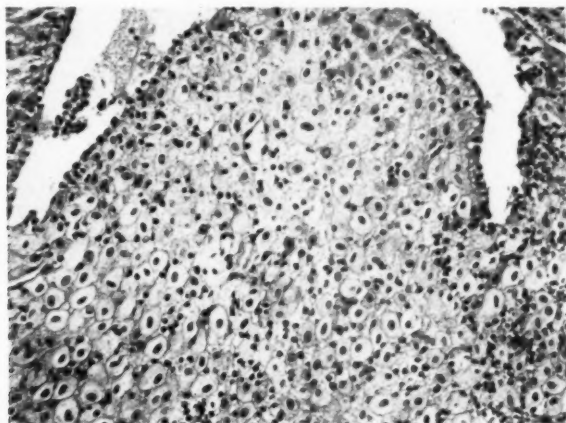


Fig. 4.—(Mag. 100x.) Uterine curetting in degenerating tubal pregnancy. (See Fig. 3.) Decidua intact.

Concerning the relatively frequent occurrence of vaginal bleeding in extrauterine pregnancy (in 39 per cent of the cases observed by Dr. Bubis³) the impression is gained from a study of 17 curettings in this series that it probably depends upon changes other than the casting off of uterine decidua. In only 5 of the 17 cases was decidua found in the curettings. In 2 cases the stromal cells were

swollen but were not typically decidual in type. In 7 the appearance was that of interval endometrium, and in 3 the picture resembled that of premenstrual endometrium; a few showed some inflammation and one an early polypoid change. In the majority of these cases there was vaginal bleeding which at times was profuse. The bleeding was least marked in the cases with decidual tissue in the curettings and most profuse in those with none in the curettings but with intact decidual tissue and intact chorionic villi in the tube.

CONCLUSIONS

In a study of 74 cases of extrauterine pregnancy, evidence was found for the belief:

1. That a decidual reaction of greater or less extent occurs constantly at the site of implantation.
2. That the decidual tissue persists as long as the chorionic villi are intact.
3. That following the termination of the pregnancy by hemorrhage with resultant degeneration of the chorionic villi, the local decidual tissue undergoes involution.
4. That a distant decidual reaction in other portions of the tube, uterus, or elsewhere is not constant, and that when it does occur, it may persist after the degeneration of the chorionic villi and the complete involution of the local decidual tissue.
5. That the relatively frequent occurrence of vaginal bleeding in extrauterine pregnancy probably depends upon changes other than the casting off of uterine decidual tissue.

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After a colpotomy a mass of tissue was found in the vaginal vault which resembled a papilloma; however, after removal it was found to be a fallopian tube. The author points out that intravaginal prolapse may be found after two operations; namely, colpotomy and vaginal hysterectomy with conservation of the adnexa. The accident apparently is rare, because the author could find no reference to it in either the French or the German literature. Kelly, however, describes it explicitly in his *Operative Gynecology*.

J. P. GREENHILL.

IMPETIGO OR PYODERMATITIS NEONATORUM*

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HISTORY.—Tilbury Fox described the contagious impetigo of children and infants in 1864. He called attention especially to the vesicular form which now appears in our maternities. Almquist, in 1891, showed that the infecting organism was a staphylococcus. Matzenauer, in 1900, linked pemphigus neonatorum to impetigo contagiosa by proving the identity of the activating microbe. Animal inoculation generally failed but in 1911, Landsteiner and his associates produced pemphigoid lesions in the chimpanzee.

With these several discoveries the knowledge of impetigo remained about stationary until 1917. Curiously enough no widespread epidemic called any particular attention to the disease in the fifty-three years that elapsed after its recognition by Fox. In 1917, however, as our questionnaire verified, this affection hitherto rare and sporadic, suddenly changed its type and appeared in more or less virulent epidemics. Very few maternities were exempt and some of us who had had no experience with impetigo as a nursery problem, were overwhelmed by the flood of cases. Everywhere our nurseries were treated like contagious disease hospitals but only with partial success. Many were closed entirely and others should have been.

Dr. F. H. Falls, finding himself in the presence of a serious outbreak, identified the disease by the organism and filled with laudable zeal proved his diagnosis by autoinoculation which in twelve hours resulted in a vesicle from which he cultured again in forty-eight hours the staphylococcus.

Such a history inspires questions and speculation. Why should a disease which has been quiescent for over half a century, as the literature indicates, take on at a particular time the epidemic form and appear simultaneously all over the country? Again, why should a hospital like Wesley Memorial, in which the infection has never been seen, abruptly encounter five visitations in a period of ten years, epidemics which spread over a term of one or two months each? We can only speculate.

The immunity of the mother and the baby was undoubtedly diminished but why and how? Was it due to the emotionalism of the war? Was it an increase of carbon monoxide in the air? Was it some change in food like a lack of carbohydrates or did the ever present staphylococcus change in type or virulence?

*Read at a Meeting of the Chicago Gynecological Society, March 16, 1928.

The purpose of this paper is to call attention to these unanswered questions and to report a hitherto questionable factor in the etiology.

Bacteriology.—It has been shown by Matzenauer and confirmed by all subsequent observers that the activating organism in impetigo is usually a peculiar strain of *Staphylococcus aureus* or *albus*, though other bacteria like the *streptococcus* are encountered occasionally. Our own experience coincides with this conclusion which has been ably discussed and summarized by Belding.

That the organism is not always the same in character and potency is urged by Baerthlein, who isolated four distinct types of staphylococci from one bleb. His work seemed to show that the diversity of type was due to variability within species. It is also Mellon's opinion that the staphylococcus and streptococcus are saprophytic most of the time but have "cadences of virulence" in which impetigo is one pathologic manifestation.

Microscopically as well as macroscopically the blebs show many diversities. Some are sterile and some are not. In the congenital cases reported by Labhardt and Waltart in 1908, some of the vesicles contained no microbial elements but did show white cells, and some polynuclears. Our own findings in congenital cases were similar except in two instances.

Nomenclature.—The bullous exanthema which occur in the course of many septic conditions may be symptomatic of the same underlying cause in pemphigus or merely a kindred phenomenon but it is more rational to consider the mild pemphigus of the newborn as closely allied to what is termed impetigo contagiosa. Many observers accept this and McCandlish further suggests that dermatitis exfoliativa, through its staphylococcus origin, belongs in the same category, though probably a more malignant form. Multiple abscess, which is frequently associated with the just mentioned diseases, has also the staphylococcus as its causative agent. Since the histologic findings are essentially identical in all these diseases which show a common origin, it is justifiable to assume that pemphigus, impetigo, multiple abscess, and dermatitis exfoliativa when occurring in the newborn are parts and phases of the same affection though in this we go somewhat farther than Matzenaur and McCandlish have indicated. All are due to the staphylococcus or streptococcus or both, and all may appear at the same time on the same individual; the variations in the clinical picture being due to different strains or different combinations of the invading organisms together with differences in soil, in resistance and in the idiosyncrasy of the patient.

In one case of congenital impetigo hereinafter reported the baby was born with impetiginous pustules on the scrotum, developed blebs of pemphigus on the hairy scalp and a circumscribed collection of

fluid under the scalp. Thus three aspects of the disease with only one evident etiology were present in the same individual at the same time.

If we admit the force of the data presented it would seem best to separate these diseases which belong distinctively to the newborn from those similar affections in older children which do not always have the same clinical appearance or etiology (Belding). The infections of older children are well established in the professional mind as pemphigus, impetigo, and multiple abscess, and we propose that this kindred group of skin infections in the newborn which has been confused by inappropriate, indistinctive, and misleading names be henceforth combined under one specific designation.

We therefore suggest the name of pyodermitis neonatorum because it is descriptive of the histologic findings. To be sure, this term combines a Greek noun with a Latin qualifier but both are the tongues of science. Adjectives like contagiosa, benigna, and maligna can be added if necessary for completeness. Thus we have the following:

Definition.—*Pyodermitis contagiosa neonatorum*, an acute contagious inflammatory disease of the newborn infant, characterized by discrete, flat, umbilical, superficial blebs or vesicles on a mildly hyperemic base, which contain a clear, an opalescent fluid or pus and tend rapidly to subside or to rupture with consequent exfoliation of the skin, or to develop further into subdermal abscesses.

Morbidity.—The seriousness of the disease manifestly depends on the severity of the attack and the susceptibility of the baby. It is probable that in general 30 per cent of all babies exposed will show signs of the infection. Belding gives 20 to 30 per cent and Dickey 34 per cent. The mild cases are self limited, with a cycle of about twelve days. The health of the baby is not materially affected. There are no constitutional symptoms. The virulence of the germ is slight. The baby is well nourished and usually fever free. On the other hand, if the child dies, a higher potency of the invading organism must be suspected. That death is not rare in the graver forms is shown by several observers. Thus in Biddle's epidemic 30 per cent died. Cole and Rue lost 1 out of 9 cases; Schwartz 25 per cent and Hartzell 50 per cent. Falls had 2 deaths in 47 cases and McCandlish 1.3 per cent. Belding's average taken from 15 observers is 21 per cent.

Transmission.—Since the staphylococcus usually and the streptococcus sometimes is the etiologic factor, how does the child get the disease? The babies themselves give no clue, for the well nourished are affected as frequently as the weaklings. Indeed male and female, fat and lean, premature and postmature, and babies spontaneously or instrumentally delivered are all attacked equally. In Waltart's case one of a pair of twins was born with impetigo while the other was clean and remained so.

The five most obvious means of conveying the contagion are: the attending physician or nurse, other infants, the paraphernalia of the nursery and the mother.

The physician is undoubtedly a carrier. The unclean obstetrician, the gynecologist whose hands are daily plunged into suppurative pelvic organs, the general surgeon who handles pus cases, the interns who dress them, and the general practitioner who is compelled to attend illnesses that are openly or only possibly septic, cannot exonerate themselves from guilt if they take on obstetric work or enter the nursery or handle the babies without the most elaborate antiseptic precautions. Young children and other lay visitors to the nursery are even more liable to be carriers, for the staphylococcus is everywhere.

A healthy infant can easily be contaminated through direct or indirect contact with other babies either before or after the signs of the disease have appeared. Again the infected baby may infect its mother or nurse, as Falls reports, and these in turn will spread the epidemic. In Abegg's case of congenital pemphigus the baby died on the second day but an epidemic in the nursery followed.

The nurse is in constant attendance on the babies and may have the organisms on her person as an acne, a suppurating antrum or a chronic nasal infection. At other times she may carry the infection from one baby to another or from septic contacts elsewhere. Relief nurses are especially apt to carry contagion into the maternity.

The utensils in the nursery may be at fault. The clothing, bedding, and linen can be autoclaved and made reasonably safe but certain objects may escape the most painstaking efforts. Thus Dickey, after providing his babies with what he thought was a definitely sterile environment, tested his precautions by culture and got positive growths of staphylococci from the scale tray, from the towel over the tray, from the bath thermometer, the table drawer, and the water from the shower.

Mothers with erysipelas, acute abscesses, cellulitis, and impetigo obviously may be a source of contamination to the baby. A breast with staphylococci in the gland tissue or in the milk may start a widespread epidemic.

Mellon and his associates made cultures of the maternal milk from the superficial ducts and from the deeper recesses of the breasts and demonstrated the staphylococcus. In tracing epidemics this possibility must not be overlooked. Apparently the so-called normal human milk contains a varying percentage of staphylococci. Mellon states that probably 30 per cent show positive cultures and yet mastitis does not occur nor do the babies necessarily have pemphigus. He also states that the organism can be present in the blood stream with few or no symptoms.

Kostlin claims the staphylococcus is present in the milk of 23 per cent of pregnant women while Cohn and Neumann will admit only 2 per cent or less. In the milk of 137 puerperal women examined by Kostlin, he found the *Staphylococcus albus* in 132 and the *Staphylococcus aureus* in 79. In response to our questionnaire, the Nebraska Methodist Hospital reported that the breast milk from all but one of the mothers of their infected babes gave positive cultures of staphylococcus.

Making all allowances for errors in these data we must agree with Mellon and regard the breast milk as one probable source of infection. Naturally it can be excluded where the baby does not nurse and where the eruption occurs before the baby goes to breast. In two of our own cases, breast abscesses developed and the babies broke out with pustules so nearly at the same time that it was impossible to say which infected the other or whether both were due to some common source like the milk.

It is evident that after the child is delivered, the opportunities for contamination are innumerable but what shall we say about the congenital cases? Must we consider these as cryptogenic infections wherein no port of entry can be discovered?

In the series of congenital pemphigus and impetigo reported by Labhardt and Waltart we get no clue to the origin of the infection. No milk or blood cultures are reported. One mother had phlebitis before confinement and may have had organisms circulating in the blood at the time of labor. It is possible too that many of the pemphigoid blebs are due to toxins from angina, influenza, or other similar infections. Nevertheless, most of the mothers in the Labhardt series were apparently in good health even where the streptococcus was found in the bleb. Even so we cannot exclude a blood contamination with placental transmigration.

Infection from the vagina could occur if the interval between the rupture of the membrane and the delivery was long enough but this was possible only in one instance. Von Reuss states that healing lesions have been found on the newborn infant which can only be interpreted as proof that infection occurred before the rupture of the bag of waters. If the blebs are explained as a product of an obscure toxin in the mother or baby then the pustule must be due to some endogenous agent. If the mother furnishes the germ there are still two barriers to be passed, the placenta and membrane whether injured or uninjured. Spirochetes, tubercle bacilli and the germs of variola and scarlatina can pass the uninjured placental wall. That other bacteria can also be carried through by the blood stream we must assume and the more readily if the filter is defective. Hellendall claims that bacteria from the peritoneal cavity can penetrate the uninjured membrane by way of the tubes but again we are moved to

ask how the organisms can reach the baby if the liquor amnii is sterile as Raineri demonstrated in 1907? Does a sterile liquor amnii sterilize also a pustule or bleb arising from a blood borne infection?

Congenital Infections.—Admitting contamination by contact from nurse, mother, doctor, nursery paraphernalia, and the milk as well as from other babies, we still have cryptogenic cases and the congenital infections. Labhardt and Waltart report sixteen instances of congenital pemphigus or impetigo. In response to our questionnaire the Fifth Avenue Hospital of New York, reports two more "discovered before the cord was cut." To these eighteen we desire to add nine cases which have appeared in the Wesley Hospital Maternity since 1925. It is probable that many were overlooked prior to this date.



Fig. 1.—Congenital impetigo from *Streptococcus hemolyticus*.

The babies in this series all showed distinct blebs or pustules. The two that came first slipped by us with notation only for we were not familiar with Labhardt's work and regarded the event dubiously. The next seven came along at irregular intervals. The blebs and pustules on five were sterile. We found only leucocytes, some being polynuclear, as signs of inflammatory changes and microbial activity. Whatever germs had been present had perished and undergone absorption. From the pustules of one, however, we obtained a positive culture of staphylococcus. Thus out of these eight cases only one was unimpeachably diagnostic.

This was the situation when on February 9, 1928, Baby H. was born in the service of Dr. Hauch by whose courtesy this report is allowed. The child was

a male, about three weeks overdue and weighed ten pounds and fourteen ounces. He was delivered at 5:08 A.M. and examined immediately. A slight hypospadias was present on an otherwise fine body. On the swollen scrotum were fifteen umbilicated pustules varying in size from 2 mm. to 5 mm. These pustules were deep yellow in color and apparently undergoing retrograde metamorphosis. The field of infection was photographed by Dr. Mason. The Kahn test and Wassermann were done on mother and baby, and smears and cultures made from the pustules by Dr. Thurman. Twelve hours after birth the hairy scalp was covered with small pemphigoid blebs. Twenty-four hours after birth, a large subdermal fluctuant mass appeared over the left parietal bone. Thirty-six hours after birth several punctate yellow-headed pustules developed on chest and abdomen.

The Kahn test and Wassermann were negative for mother and baby. The cultures made from the blebs, from the fluctuant subdermal mass on the scalp, and the secondary pustules on the chest and abdomen were negative. The culture of the primary pustules on the scrotum gave a positive growth of *Streptococcus hemolyticus*. The child was fever free, nursed well, and gained weight. On the eighth day an indurated nodule as large as a bean appeared on the left cheek. This also, after eight days, subsided without suppuration which suggests that the immunity had become generally established. The mother gives a history of tonsillitis four weeks prior to delivery.

The milk appeared in the mother's breasts at the usual time and upon withdrawals of specimens by Mellon's technic it was found that all the fluid, deep and superficial, gave almost pure cultures of *Micrococcus tetragenes*.

Belding states that no etiologic relationship has been established hitherto between the streptococcus and so-called impetigo contagiosa. This, therefore, must be the first report of an obviously uncontaminated case due to the *Streptococcus hemolyticus*. The streptococcus, according to report, is extremely rare as the sole activating organism. To speak further than this would be mere speculation.

This case has awakened a new interest in the neglected and almost forgotten pioneer work of Labhardt and Waltart and by emphasizing the possibility of intrauterine infection gives us a new factor in the etiology which must be reckoned with hereafter when epidemics arise.

Prevention.—Prophylaxis in the maternity took on an extreme aspect when the first epidemic of impetigo visited Wesley Hospital in 1917. The walls, tables, cribs, and woodwork were scrubbed with soapsuds, wiped off with cresol solution and repainted. The linen, bedding and all movable utensils were autoclaved. Bottles, nipples, and every shred of material that touched the baby were twice sterilized. The tub baths were given up and a slab and spray system installed. Albolene, borated lard, and other unguents which were regarded as essential for the removal of vernix caseosa were abandoned and sterile green soap from sterile containers was employed. Babies were not handled except for washing, changing, and taking to breast and then by nurses who passed their hands through chlorine or bichloride solutions between each case. Frequent inspection of well infants was observed to provide for prompt quarantine. In every instance where blebs or pustules appeared they were opened with aseptic

care, treated, and the baby isolated under the care of a special nurse, who handled the case with gloves. Whether these precautions made any difference in the spread of the disease we cannot say, for epidemics came and went.

Treatment.—The active management of our first infections followed the methods ordinarily successful in older children. We began with ointments like ammoniated mercury and found them useless. Where the blebs were punctured and covered with the ointment, new vesicles formed underneath. Mereurochrome and iodine were no better. Dusting powders containing boric acid or formalin helped some but dermatol was too harsh on the skin when continually applied. Meanwhile the blebs were opened by a sterile needle or by a pledget of gauze soaked in 95 per cent alcohol and the pustules and abscesses were iodinated and opened with antiseptic precautions. At the present time all the spots of irritation, either advancing or receding, and all the opened blebs and pustules are washed with alcohol or a 1-200 solution of hypochlorite of sodium and covered with calamine lotion. A 5 per cent or 10 per cent solution of silver nitrate is sometimes applied to the opened pustule and the quartz light is used where the pustules are numerous.

After our attention had been called to the diminished immunity hypothesis by the occurrence of the congenital infections we thought of vaccines and this brought us to the question of immunogen. Immunogen is made from the ectoplasm of the bacterial cell and theoretically has all the virtues of the vaccine without the toxin. It is an aqueous solution of the antigens of *Staphylococcus albus* and *aureus* with a trace of phenol for preservation.

Our purpose was to inject fifty consecutive cases in the general service and have the private cases as a control. This study was carried out with conscientious thoroughness by our resident obstetrician, Dr. Thurman. In all we injected forty-eight babies but two were withdrawn from the series after two injections because one was found to have an enlarged thymus and the other developed projectile vomiting. Out of the forty-six injected babies, seven showed pustular eruptions on the third, fifth, and eighth days but they all cleared inside of two days. Thirty-nine, or 80 per cent, were untouched by disease.

During this period twenty-seven private cases passed through the maternity without immunization. Twenty-four of these, or 88 per cent, had pustules. The epidemic now ceased and the experiment was discontinued.

Conclusions, of course, are impossible from such scanty data but according to our present hypothesis it would seem that a certain proportion of the babies become infected in utero and the pyoderma-

tis passes through its various stages to recovery as the healed lesions reported by von Reuss would indicate.

In the next degree it is found on careful examination that vesicles or pustules exist at birth. The outbreak, however, is stationary or retrogressive. Some of the older eruptions will contain germs, but since immunity was practically established at the date of delivery the new blebs that develop do not become infected. The subdermal accumulations of fluid as well as the indurated nodules are aborted in their evolution. Suppuration does not occur in any of these foci and the skin rapidly clears. This theory is supported by the fact that so many of the earlier lesions in our series and in Labhardt's were sterile together with the clinical picture presented in the case of congenital pyodermatitis on which this paper is based.

At other times, the infections in utero of later onset may continue in a state of active inflammation up to the birth. Now the pemphigoid vesicles break out on or before the third day of life as a result of the circulating toxin. The contents become infected, pustules form and the disease may pass on into the multiple abscess stage with positive germ cultures at all times demonstrable. Meanwhile the baby is constantly a potential source of contamination to other individuals as Abegg's case exemplifies.

Where the blebs and pustules are not of congenital origin the eruption must break out as late or later than the second day as Fall's autoinoculation proves. These babies which break out on the third day or later are infected by the milk, by contaminated apparatus, by other babies or carriers. In every case of this kind the milk should be suspected and cultured by Mellon's technic.

The rather surprising results of the immunogen experiment would indicate that diminished immunity is a very pronounced factor in the contagion and while none of the prophylactic measures hitherto described can be neglected, yet the evidence strongly indicates that success in prevention can be completely achieved only by raising the resistance of mother and baby to a point where pyogenic organisms cannot live.

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(For discussion, see page 133.)

REPORT OF A CASE OF PLACENTA ACCRETA; WITH A DISCUSSION OF ITS TREATMENT AND THE UNUSUAL SEQUELAE*

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IN REPORTING and discussing this case of placenta accreta I feel I may aid in further clarifying our conception of this condition, particularly its treatment. The sequelae to be described are rare and, for this reason, worthy of presentation.

Mrs. A. F., age thirty-four, para iii, entered the Methodist Episcopal Hospital, October 10, 1925.

The family and past history were negative, and two previous pregnancies were without complications. Two weeks before admittance the patient gave birth at home to a full-term child; the delivery being spontaneous and without lacerations. With the greatest difficulty and the use of considerable pressure, the placenta was delivered one hour later, and as one cubic centimeter of pituitrin had been administered immediately following delivery, the difficulty was ascribed at the time to the use of this drug. The placenta was hurriedly inspected and, although rough and shaggy, appeared to be intact. On the second, fourth, and tenth days post-partum free bleeding occurred, lasting from one half to two hours. Bleeding was continuous from the tenth to the fourteenth day, the patient becoming pale and weak, and her general condition more and more serious. During this period no internal examinations were made.

Immediate examination in the hospital revealed a woman seriously ill, pale, restless, with widely dilated pupils, and a pulse rate of 130. A subinvolted uterus with some tenderness over the fundus was found. Her temperature was 98.2° F.; blood pressure, 90/50; the urine, negative; and a blood count showed 2,700,000 red cells, the hemoglobin being 40 per cent and the leucocytes 31,000 with 90 per cent polymorphonuclears.

Operation revealed free bleeding from a cervix widely open and readily admitting the examining fingers. A mass, the size of a tangerine, firm and densely adherent, was found attached to the fundus and right lateral wall. It was impossible to find any line of separation. With difficulty, using placental forceps, the mass was removed piecemeal, although considerable uterine tissue came with it, and it was only by using much care that a perforation of the uterus was avoided. Hemorrhage was profuse, which necessitated packing with mereurochrome gauze, and the patient was returned to bed in fair condition.

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This packing was removed twenty-four hours later, her condition being then so good that a previously planned blood transfusion was not deemed necessary.

The tissue removed at operation and sent to the pathologic laboratory was later reported as placenta and small fragments of uterine musculature.



Fig. 1.—Complete gangrene of the left leg, with line of demarcation. Partial gangrene of right foot with death of middle toes.

Third day postoperative: The general condition was good, but a tingling sensation, later followed by radiating pains in the left foot and ankle, had occurred. An examination showed slight swelling and some tenderness of these parts.

Fourth day: Her condition was still good, but the foot, ankle, and lower six inches of the left leg were tender, moderately swollen, slightly discolored, and cold. The pain in these parts was most severe and was not relieved by local measures.

The veins were not tender, but the anterior tibial pulse was faint, although the femoral pulse was good. A blood culture was taken and later reported negative.

Fifth day: A change in the general condition had taken place, the patient appearing pale and sick. Her temperature was 100° F.; pulse, 110, and respira-



Fig. 2.—Section of that part of the uterus from which the placenta was removed, showing the massive gangrene of the tissues. Note the well-formed leucocytic zone and the thrombosis of all the vessels.



Fig. 3.—Photomicrograph of wall of uterus, showing the well-formed leucocytic zone and the complete thrombosis of the vessels. Below the leucocytic zone the death of the tissues is complete, while above it some cell outlines are discernible, indicating a less advanced process.

tions, 36. Although the swelling of the left leg was less than on the previous day, there was a marked increase in the discoloration of the toes and foot and an extension of this discoloration to within four inches of the knee. No femoral pulse could be detected.

Sixth day: The condition of the left leg was about the same and for the first time the right foot and toes were found to be cold, slightly swollen, tender, discolored and the tibial pulse no longer present. A blood count at this time showed 2,800,000 red cells and 44 per cent hemoglobin; a transfusion of 650 c.c. of blood was given. This was followed by a chill and no general improvement.

Seventh day: The patient was much worse, complaining of severe pain in the right foot and complete loss of sensation in the left. The temperature was 103° F.; pulse, 120; respirations, 25, and blood pressure, 110/60. For the first time marked tenderness was present over the entire uterus, the involution of which was markedly retarded.

Eighth day: Her general condition was still worse, the pulse was thready, and stimulation was now being used. The left leg had become gangrenous with a line of demarcation four inches below the knee, and there were blebs on the foot and



Fig. 4.—Photomicrograph of the uterine wall, showing thrombosis of the vessels, large amount of detritus and dead muscle cells, swollen, pale and difficult to outline.

toes. The femoral pulse in the right leg was now markedly impaired, the foot more discolored, and the second and third toes gangrenous.

Ninth, tenth, and eleventh days: The patient's condition became more and more critical, the temperature remaining about 105° F.; pulse, 140; respirations, 25, and during this time the local findings showed further progression of the gangrene. Blood cultures taken on the sixth and eleventh days were later reported positive, showing a nonhemolytic streptococcus.

Twelfth day: The patient expired. A blood count taken just before death showed red cells 2,300,000; hemoglobin, 38 per cent; leucocytes, 41,000; polymorphonuclears, 90 per cent, while previous blood chemistry and Wassermann examinations had been negative.

Postmortem Examination.—Permission for this was obtained with great difficulty and solely on the condition that the examination be limited to a small incision in the abdomen and one only in the left thigh.

The parietal and visceral peritoneum were normal as were the liver, pancreas, kidneys, and other abdominal organs, with the exception of the spleen, which was moderately enlarged, soft, and friable.

The uterus was 12 cm. in length, very soft and flabby, and the fundus was adherent to a coil of intestine which was easily separated. Beneath this adhesion was a black, gangrenous area 7 cm. in diameter. The entire uterine wall was gangrenous, with the most advanced process at the fundus from which the placental mass had been removed, and the cavity of the uterus was lined with black, shaggy, necrotic tissue, thickest at the fundus. The tubes and ovaries were substantially



Fig. 5.—Cross-section of the left external iliac vessels, showing the collapsed artery and thrombosed vein.

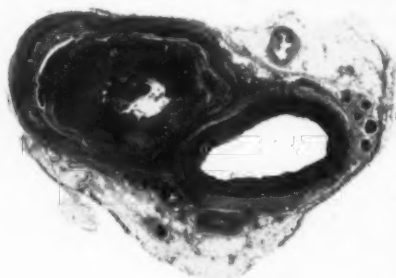


Fig. 6.—Cross-section of left femoral artery and vein, showing a thrombosis of the latter.

normal, but the pelvic peritoneum was dull, covered with a thin coat of fibrin and there were a few cubic centimeters of cloudy fluid in the culdesac.

All the veins in the broad ligaments were thrombosed. The left external iliac and femoral veins were filled with a continuous organized thrombus which was attached to the wall of the vein and could not be removed. Another antemortem thrombus, 20 cm. long, was removed from the right external iliac and femoral veins, this thrombus being apparently of more recent formation than the one on the left side. Both iliac arteries were collapsed and empty.

After cutting down upon the femoral vessels in the left thigh the vein was found to be completely thrombosed as far as it could be traced, but the artery was empty. Sections of these vessels were taken for microscopic examination.

There was slight swelling and marked discoloration of the left leg commencing four inches below the knee, with a definite line of demarcation at this point, the tissue above this line appearing healthy. The ankle, foot, and toes were also gangrenous with a few scattered blebs. The anterior surface of the right foot showed a purplish discoloration, beginning at the ankle and increasing distally, and the two middle toes were black.

Diagnosis.—Placenta accreta, gangrene of uterus, pelvic peritonitis, venous thrombosis, and gangrene of lower extremities.

This was a case of partial placenta accreta, and the question naturally arises as to whether or not the best method of treatment was



Fig. 7.—Photomicrograph of left external iliac vessels, showing the empty artery with normal intima. The vein is occluded by a well-organized thrombus, the blood clot having been completely replaced by young fibrous tissue. The intima of the vein is thickened and merges imperceptibly with the thrombus in which is also noted considerable leucocytic infiltration.

followed. Would a better result have been obtained if, upon finding that manual removal of the placental fragment could not be done without damage to the uterine wall, the uterus had been packed and a subsequent hysterectomy performed? I believe that an affirmative answer to this question, while naturally impossible of proof, is reasonable. Numerous writers have shown the dangers of manual removal in this condition. We should not confuse the ordinary adherent placenta with a placenta accreta. In the former there is simply a failure to separate for various reasons, such as failure of the uterus to contract properly, as in atony, or implantation of the placenta over a

noncontractile portion of a uterus, as in cases of large intramural fibroids. In placenta accreta, we often find a history of endometrial disease, adherent placenta or repeated curettages, and because of the previously damaged or atrophied endometrium, the decidua basalis is thin or absent and the villi penetrate deeply into the uterine wall and are in intimate relation with the muscle fibers. It is evident that placental separation over this area is impossible, as the normal spongy layer does not exist. Hirst states that adhesions of the placenta to the uterus occur once in every 312 cases, but that they are usually slight and manual removal is easy, while Polak places the incidence of placenta accreta about one in 6,000.

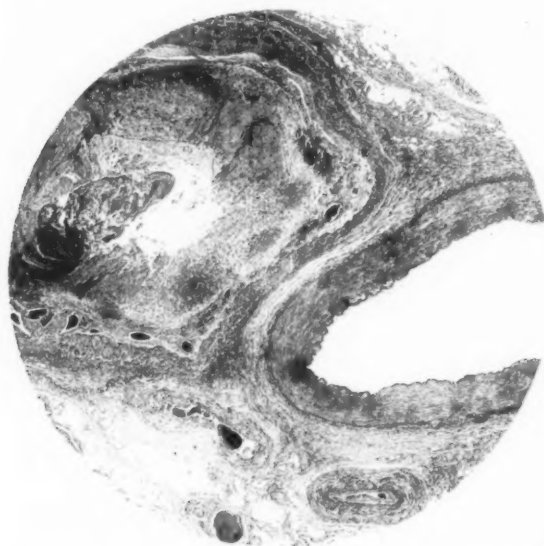


Fig. 8.—Photomicrograph of the left femoral vessels, showing a normal artery and a thrombosed vein. This thrombus is of more recent formation than that in Fig. 7, consisting principally of blood clot with a few new capillaries near the intima. Organization is just beginning.

Despite occasional good results I feel that, in view of our knowledge of the pathology of placenta accreta and the dangers incident to its manual or instrumental removal, there is little justification for this course, and, once the diagnosis is confirmed, the uterus should be packed when necessary and hysterectomy then performed.

Complete gangrene of the uterus is very rare, a search of the literature of the last fifteen years showing only one such instance. This followed an attempt at criminal abortion and was reported by Fort in 1912. The uterus had been severely traumatized and, through the resulting gangrenous tissue, a six and one-half months' fetus had been extruded into the peritoneal cavity. A subsequent Porro operation failed to save the patient's life.

Gangrene of the extremities, following parturition or pelvic operations, is mentioned in the textbooks and fairly frequently in the literature and is of considerable interest. Wormser, in 1904, reported 58 cases of puerperal gangrene of the lower extremities, in which he found the arteries alone involved in 40 cases, the veins in 13, and both in 5. Stein, in 1924, published a most interesting paper on this subject, which brought out the following points: (a) It is always difficult to know the seat of obstruction from the symptoms and physical signs, but an early onset following delivery or operation is most likely to be of arterial origin and a late onset venous; (b) a rapid onset with pallor and an absence of swelling indicates an arterial lesion, and produces a dry gangrene; (c) a sudden onset, with marked edema and cyanosis, shows a venous block and produces a moist gangrene, but, if the onset be more gradual and the swelling only moderate, with a slight discoloration, it is then difficult to be sure of the seat of the thrombus.

The symptoms are quite similar whatever the etiology of the obstruction may be; a sensation of "pins and needles" followed by severe shooting pains and then pallor, or cyanosis, is finally followed, in a varying length of time, by death of the parts. A disappearance of the arterial pulsations takes place more or less rapidly due to actual blocking of the artery by the thrombus, or, in those cases in which the veins are diseased, by the inability of the blood to return, thus indirectly obstructing the arteries as effectively as if an actual thrombus were present in them.

The prognosis is always grave and, even if the condition of the patient permits amputation following the appearance of a line of demarcation, a mortality rate of 60 per cent is to be expected. Embolectomy has been attempted in a few instances and, in those cases in which the seat of the thrombus was known and immediate operation performed, there have been a few successful results following the removal of the thrombus and the washing out of the artery. In indicated cases it is justified and can later be followed by amputation if it fails.

In the case just reported, infection was undoubtedly present in the uterus before the patient entered the hospital, but was probably held in check by a well-formed leucocyte zone. Following the destruction of the latter, however, by the operative trauma, an extensive infection of the uterine sinuses occurred with a resulting thrombophlebitis. This spread to the veins, causing a block of the circulation and a resulting gangrene of the uterus. Further spread by extension of the thrombi to the numerous veins in the pampiniform plexus and then to the external iliac and so to the femoral veins then ensued; first, on the left and later on the right side. Only at autopsy, however,

were we sure of the seat of the obstruction, for we had believed the trouble to be in the arteries. The blood stream infection probably occurred secondarily, due to the contact of the blood with the infected thrombi.

Because of the strict limitations imposed for the autopsy, the further tracing of the pelvic vessels and their branches was not attempted. A study, however, of the venous system of the lower extremities and pelvis leads us to conclude that, although a guess only can be hazarded as to the extent of involvement on the right side, on the left side there was a thrombosis of the femoral, external iliac, and anterior branch of the internal iliac, but not of the posterior branch or of the common iliac veins. The tubes and ovaries were not involved because of their independent circulation; the right ovarian vein emptying directly into the vena cava and the left one into the left renal vein.

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90 EIGHTH AVENUE.

THE TREATMENT OF UTERINE INJURIES*

WITH A REPORT OF SEVEN CASES

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THE term uterine injuries is used advisedly for it is my intent to consider both perforation and rupture of the uterus. The purpose of this presentation is, first, to add to the records another series of instances of uterine injuries, and secondly, to evaluate from this though limited series of cases the result of conservative surgical treatment.

As this is a recital of personal experiences, and not a bibliographic review, I shall not burden you with statistics, except to state that A. B. Davis, in a review of 148,000 deliveries at the Lying-In Hospital over a period of thirty-seven years, found only 184 ruptured uteri.

The incidence of perforations of the uterus is more difficult to estimate, for there is no definite information on this subject. This lack of information may be explained by the fact that many cases of per-

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forated uteri are not recorded, when the puncture has been made by a sound during operation or during attempted criminal abortion.

The cases in this series may be grouped as follows: four cases of perforation and three cases of rupture of the uterus. Of the four instances of perforation, two were complicated by intestinal injuries, both due to attempted criminal abortions, one case due to the introduction of a foreign body for the purpose of inducing abortion and one case caused by attempted curettage for an incomplete abortion. Of the three cases of ruptured uteri two were during labor, one of which was complicated by the escape of the placenta into the abdominal cavity; one of these three cases was caused by attempted extraction of a large submucous fibroid. Of these seven patients six were operated upon and recovered; one patient, who had a ruptured uterus, was not operated upon, and died.

The first case of uterine injury that came under my observation was that of a woman, twenty-two years old, married, who was admitted to my service at the Jewish Hospital on September 14, 1918, with the following history: that on the morning of her admission to the hospital the patient had an abortion performed and immediately after the curettage she was seized with severe abdominal cramps. The physician who referred the case to me stated that during the curettage he pulled down a loop of small intestine into the vagina which he immediately returned into the abdomen and packed the vagina with iodoform gauze.

On admission to the Hospital, the patient's temperature was 102° , and the pulse 110; the abdomen was tender and rigid from the level of the umbilicus down. On removal of the vaginal packing, the cervix showed an old laceration with a closed external os. The uterus and adnexa could not be palpated on account of the abdominal rigidity. The physician's positive assertion that he had recognized the intestine in the vagina, and the local findings, determined my course for an abdominal exploration.

On opening the abdomen the pelvis was filled with blood and the uterus was small and presented no evidences of pregnancy. There was a perforation through the fundus about 5 cm. wide. The mesentery of a small loop of ileum was split longitudinally and detached. The peritoneal coat of the intestines was denuded in several places; the largest area measured about 7 cm. in length. The uterine perforation was repaired, and the denuded surface of the intestines was covered with the edges of the torn-off peritoneum. To such places as could not be covered by the peritoneum, a purse string suture was applied. The mesenteric rent was then repaired. Two cigarette drains were inserted behind the uterus and the abdomen closed. For two days after operation the pulse remained between 120 to 130 but the temperature not higher than 100.6° . The drains were removed on the third day, but on the fourth day the temperature rose to 102° , the pulse remaining at 100. The patient's temperature persisted at 103.6° for two days, then dropped to normal. The patient was discharged on the fourteenth day after operation with a well-healed abdominal wound excepting for a small granulating area at the site of the drains. The uterus was slightly enlarged, in good position, rather fixed, and the pelvis free of any exudates. This patient was seen in December, 1919, when she complained of lower abdominal pain. The uterus was dextroverted and moderate bilateral parametritis was present. Under appropriate treatment, the parametritis resolved. August 27, 1924, she again con-

sulted me stating that in 1920 she had had a spontaneous, six months' miscarriage. The findings at this time showed a dextroverted uterus but no parametrial involvement.

The second case of uterine injury that came under my observation is that of a young woman, twenty years old, married, who was admitted to my service at the Jewish Hospital on January 12, 1920, with the following history: that on the morning of January 12 she had a curettage performed. In the course of this procedure a placental forceps was inserted into the uterus for the purpose of removing the products of the undesired conception, but the operator was unhappily confronted with the victim's entrails presenting in the vagina. He immediately stopped the operation and packed the vagina with iodoform gauze. I saw this patient at the physician's office within half an hour after the occurrence of this accident. The patient complained of slight abdominal cramps, but otherwise was apparently comfortable. She was transported from the doctor's office in an automobile and without any discomfort walked up the flight of stairs leading to the hospital.

On admission the temperature was 97° and the pulse, 100; the abdomen was flaccid and sensitive in the pelvic zone. The W.B.C. was 19,000 with 89 per cent polys; R.B.C. 3,850,000 and 80 per cent hemoglobin. After an antemortem statement had been obtained for legal purposes, the patient was taken to the operating room.

On removal of the vaginal packing a loop of discolored small intestine was found in the vagina. The diagnosis now being obvious, the abdomen was immediately opened through a median incision. There was no blood or free fluid in the peritoneal cavity. The uterus was enlarged and was perforated to the extent of 3 cm. in the right border of its anterior aspect about the level of the internal os, and a loop of almost gangrenous intestine had been pulled through this opening. The continuation of this loop of bowel was detached from its mesentery and measured 60 cm. in length. The anterior blade of the right broad ligament was torn to the extent of 5 cm. involving the anterior peritoneal reflection of the bladder. The loop of intestine was then extricated from the uterine opening and the mesentery ligated. The intestine was clamped at both ends of the loop and resected. The free ends were then ligated and inverted with purse-string sutures, and a side-to-side anastomosis performed. The uterine wound was sutured and covered by the bladder peritoneum. Two cigarette drains were inserted behind the uterus.

Postoperatively, the temperature ranged between 99° and 101° for the first five days, then rose to 103° for a few days. One drain was removed on the second day, and the other about the fifth day. There was a very profuse discharge from the wound which gradually subsided and the wound was completely healed at the time of the discharge. Ten days before discharging the patient, an x-ray study of the gastrointestinal tract revealed that there was no evidence of local stasis, pocketing or angulation.

On discharge, the abdominal wound was healed except for a small sinus at the lower angle; the uterus was small, retroverted and fixed by an insensitive exudate at the base of the right broad ligament.

The interesting features of this case are: first, the extent of the injury; second, the comparative comfort and lack of symptoms; third, the magnitude of the operation; and fourth, the conservation of the pelvic organs.

Of the two cases of perforation of the uterus without intestinal injury, the first one was that of a woman, thirty-three years old, married, para iv, who was admitted to the gynecologic service of the United Israel-Zion Hospital on November 15, 1923, with the following history: she expected her menstrual period on November 19, 1923, and being disappointed by its nonappearance, was led by fear

of pregnancy to insert an ivory crochet needle into the cervix. During this experiment she suddenly felt the needle slip from her hand. Soon after the accident a bloody vaginal discharge appeared and persisted. Excepting for occasional abdominal cramps and pain in the vagina on walking she experienced no discomfort. On the day prior to her admission to the hospital she had one chill.

On admission her temperature was 100°; pulse 90; blood count showed total white cells, 9,200 and 79 per cent polynuclear cells. Examination revealed moderate tenderness in the lower part of the abdomen; a lacerated pelvic floor and cervix; and an anteflexed, retroverted, soft uterus with sensitiveness in the left fornix. On the second day at the hospital her temperature dropped to normal and remained so. Because of the absence of marked abdominal symptoms and the element of doubt concerning the disappearance of the crochet needle into the abdominal cavity, the patient was kept under observation for several days. On November 18, a bedside radiographic examination revealed an indefinite shadow in the right iliac fossa. The radiographist, being in doubt as to the correctness of the plate, advised another examination. On November 25, a second x-ray examination revealed a definite, long shadow in the right iliac fossa. There being no doubt now as to the presence of the crochet needle in the abdominal cavity, an operation was advised. Repeated bimanual examinations without anesthesia as well as bimanual examinations under anesthesia failed to confirm the presence of a foreign body in the abdomen.

On opening the peritoneum an ivory crochet needle, 15 cm. long and 5 mm. in diameter, was found lying free in the abdominal cavity with its business end on the cecum and its base against the left ascending ramus of the pubis. The uterus was retroverted and from about the middle of the fundus, a single fine adhesive band, extending to the omentum and crossing the needle, was observed. The adhesive band was easily separated and a probe readily passed into the uterine cavity at this point. This evidently was the site of the perforation through which the needle had entered the abdominal cavity. The perforation was then repaired. There were no other evidences of pathology than the omental adhesion just described. This patient made an uneventful recovery.

This case presents these interesting points: first, self-inflicted perforation of a viscus by a foreign body and its escape into the abdominal cavity; and second, the absence of abdominal symptoms or infection. The latter may be due to the fact that the patient claims to have thoroughly boiled the needle before inserting it.

The second instance of perforation of the uterus without intestinal injury, occurred during a curettage for an incomplete abortion. This patient, aged thirty-one years, was admitted to the gynecologic service at the United Israel-Zion Hospital on September 19, 1927; married four and a half years; two previous cesarean sections, three and one-half and two and one-half years, respectively; a curettage for incomplete abortion about eight months ago was performed. The patient had her last menstrual period on July 19, 1927. About August 20, the patient realizing the possibility of pregnancy, resorted ineffectually to the common medicaments for artificially terminating pregnancy. About September 14, she began to bleed rather profusely. This continued in a lesser degree for about a week. On the day of her admission to the hospital, the patient had a rather severe hemorrhage for the relief of which a curettage was attempted at her home. During the course of this procedure, a placental forceps was introduced which, on removal, was found to contain a piece of omentum. The patient soon showed all evidences of shock and was immediately transferred to the hospital.

On admission the patient looked very pale, a cold perspiration covering her entire body; heart sounds were only of fair quality; pulse weak, with slight tenderness in the pelvic region. Blood pressure was 64/40; blood count showed R.B.C. 3,250,000; HGB. 50 per cent. The patient was immediately given a hypodermoclysis of 1000 c.c. of saline and expectant treatment resorted to for the relief of the

shock. Five hours after her admission to the hospital the patient's pulse was 72; blood pressure 80/46, and the blood count showed a R.B.C. 3,100,000; HGB. 65 per cent. A diagnosis was made of perforation of the uterus with injury to the omentum.

The patient's condition now warranted surgical intervention. On opening the abdomen the omentum was found in the pelvis with a few of its strands attached to the uterus. About an ounce of blood clot was removed and some fresh blood was found oozing from a wound through the peritoneum covering the anterior surface of the right broad ligament. This wound was in the anterior surface of the uterus about the level of the internal os. The perforated area was cleaned, freed from blood and the raw surface approximated with catgut sutures. The torn peritoneum was then sutured so that it covered the uterine wound. The omentum, which was traumatized, was ligated and resected. The uterus was found to be the size of about a six to eight weeks' pregnancy, quite irregular, and had two small fibroids, one in each cornu. There were two scars on the anterior surface of the uterus the results of the previous cesarean sections. The abdomen was closed without drainage. A transfusion of 400 c.c. of blood was given the patient. She reacted very well from the operation. Two days later the patient was suddenly seized with severe pain in the left chest, with difficulty in breathing. A diagnosis at this time was made of a pulmonary infarct. The following day her condition improved and continued to improve, excepting for a collection of serosanguinous fluid in the wound, which was opened and drained.

The patient was discharged on the twenty-eighth day after operation with a well healed abdominal wound, and a retroflexed uterus with an insensitive slight exudate in the right fornix.

Of the three ruptured uteri, the first case that came under my observation was a uterine injury caused by the delivery through the vaginal route, of a submucous fibroid after a spontaneous full-term labor. This patient, thirty-four years old, para v, was admitted first to the obstetric and immediately transferred to the gynecologic service at the Jewish Hospital, on December 14, 1918. The history of the patient is that on the night before admission to the hospital she had a precipitate labor. About half an hour after delivery she was suddenly seized with cramp-like pains in the lower abdomen simulating labor pains and accompanied by a rather brisk hemorrhage.

Examination on admission revealed a fundus reaching to about three fingers' breadth below the umbilicus, very firm and somewhat irregular. Vaginal examination disclosed a submucous fibroid presenting itself through a completely dilated cervix. The admission temperature was 100°, and the pulse 120. Blood count was 30,800 total white cells; 86 polys; 12 lymphocytes; 2 eosinophiles; total red count, 3,330,000; hemoglobin, 55 per cent.

The patient was given a blood transfusion of 750 c.c. and with the aid of repeated doses of pituitrin she extruded the fibroid into the vagina. Vaginal examination at this time showed that the fibroid had passed through the cervix and presented itself in the vagina. Her general condition having improved considerably, it was now thought best to remove the tumor. On the following day, the patient was taken to the operating room, and by gentle traction from below and pressure from above, a degenerated, submucous fibroid, ovoid in shape, 14 by 8 by 5½ cm. was delivered. Immediately after the removal of the tumor a tube and ovary appeared in the vagina. On digital exploration of the uterus a large tear in the right side was found. The abdomen was immediately opened and the uterus found to be enlarged with a rent beginning at the right cornu and extending downward along the lateral wall for a distance of about 7 to 8 cm. A total hysterosalpingo-oophorectomy was rapidly performed.

The patient's convalescence was a rather stormy one, the temperature, with slight variations, persisting at 103.5° and the pulse running from 120 to 140. The blood count was 28,000 total white cells; 88 polys; 12 lymphos; 2,250,000 red cells; HGB. 55 per cent. This condition continued for about five days. On the sixth day postoperative, an infected wound was opened and drained, following which both the temperature and pulse gradually came down to normal. On about the eighth day postoperative, a second transfusion of 350 c.c. of citrated blood was given. The patient's recovery thereafter was rapid. She was discharged on the twenty-third of January, 1919, the thirtieth day after operation.

The condition on discharge presented a well healed abdominal wound, a multiparous introitus and a well healed vaginal stump which was held up high, and a pelvis free from exudates.

This patient consulted me in 1923 at which time she was suffering from a tapeworm and excepting the usual menopausal syndrome, the physical findings were negative.

After reviewing the postoperative course of this case the question presented itself whether a repair of the injury would have resulted not only in a smoother convalescence but also in retaining the female organs where nature intends them to be. This consideration has guided me in the management of the subsequent cases.

The second case in this group is that of a ruptured uterus after a spontaneous full-term delivery which was not operated upon. This patient, thirty-five years of age, was admitted to my service at the United Israel-Zion Hospital on November 27, 1922. The history, as obtained from the family physician, is that she had four previous labors, all ending in instrumental deliveries, although none of the babies were over seven pounds. The patient had been in active labor for over four hours before the arrival of the physician at 1:30 A.M. on the twenty-fifth of November, 1922. He found that the cervix was fully dilated and the membranes intact. During his vaginal examination the membranes ruptured, about five gallons liquor amnii escaped, and a breech presented. The patient was given one-half c.c. of pituitrin hypodermically. According to the physician's statement about two and one-half hours elapsed between the administration of the pituitrin and the expulsion of the baby. The breech was delivered without any difficulty. As the baby was anencephalic there was no difficulty encountered in the delivery of the after-coming head. About five minutes following the expulsion of the child the placenta was easily expressed. No undue bleeding was noticed.

A few minutes following the expulsion of the placenta the patient suddenly complained of faintness and shortness of breath. Her condition became very alarming. She was placed in the Trendelenberg posture and given morphine, following which her condition improved. The same day the patient complained of epigastric distress. Her pulse, which had previously been imperceptible, was now 96. I saw this patient that evening and found her very comfortable, except for a complaint of slight pains in the right side of the lower part of the abdomen. The pulse was 90; slight tenderness in the right iliac fossa; lochia was normal, and rectal examination revealed a closed cervix and a well contracted uterus with some sensitiveness in the right fornix. A diagnosis of a possible incomplete tear in the lower part of the right side of the uterus was then made and expectant treatment advised. On November 27, the patient began complaining of abdominal cramps which were accompanied by vomiting.

On admission to the Hospital, the temperature was 102.4°; pulse, 160; heart sounds of very poor quality. Examination revealed marked abdominal distension with visible peristalsis; marked tenderness in both flanks with rigidity in the

outer part of the right rectus. The vomitus was yellowish in color without any odor. Vaginal examination showed a slight bloody discharge; cervix patent, admitting one finger; uterus firm and to the left. Blood examination was R.B.C. 2,080,000, W.B.C. 8800, polys 79 per cent, HGB. 30 per cent. A diagnosis of ruptured uterus was now made but surgical intervention on account of the patient's condition considered inadvisable. Her condition improved somewhat for the next twenty-four hours, then she suddenly began to bleed per vaginam. A transfusion of 250 c.c. of blood was given but her condition rapidly grew worse and the patient expired; this was the fourth day after the occurrence of the accident.

Postmortem vaginal exploration revealed a large rent in the right lateral uterine wall with a loop of bowel protruding. There was considerable blood in the peritoneal cavity.

The cause of the rupture in this case may be ascribed to the over-distension of the uterus by the hydramnios aided very likely by the administration of pituitrin.

It seems to me now that despite the risk of infecting a patient it would be wiser in cases where uterine injury is suspected to explore the uterus even in the absence of ideal aseptic conditions. An early diagnosis in this case followed by prompt treatment may have saved this patient's life.

The third case in the group of ruptured uteri was complicated by the escape of the placenta into the peritoneal cavity. This patient, twenty-nine years old, was admitted to my service at the United Israel-Zion Hospital on May 19, 1924. She had had two normal pregnancies and deliveries, eleven and nine years ago, respectively. Her last menstrual period occurred on the fourth of September, 1923, making the estimated date of her confinement on or about June 11, 1924. Three days prior to her admission the patient was delivered of a premature still-born infant. The placenta was retained; and, since there was no undue bleeding, no attempt by intrauterine interference or external manipulation was made to deliver it. On admission to the hospital, the patient was found to be in poor condition. The temperature was 102.2°, her pulse 120. The abdomen was distended and sensitive, and she suffered from continuous retching and vomiting. On rectal examination the cervix was found about two fingers dilated, and in the lower uterine segment a soft mass was palpable which was taken as the retained placenta. The lochia was scant and malodorous, and there was no excessive bleeding. The ligated end of the cord presented at the vulva. A diagnosis of retained placenta and pelvic peritonitis was then made.

The following day a transfusion of 560 c.c. of blood was administered. The blood count was 4,232,000 R.B.C.; 60 per cent HGB.; 18,000 W.B.C.; 88 polys, and 12 per cent lymphos. At this time the umbilical cord could not be seen at the vulva nor in the vagina. The mysterious disappearance of the cord and the patient's condition determined the necessity of immediate exploration of the uterus for the purpose of removing the retained placenta.

The patient was taken to the operating room; and, on vaginal examination, it was found that the cord had retracted beyond the cervix and that there was free fluid in the culdesac. A posterior colpotomy was performed which resulted in the escape of free blood from the pelvic cavity and demonstrated the presence of the placenta in the abdomen to the left and posterior to the uterus which had a tear along its left border. The culdesac was drained with iodoform gauze and a diagnosis of ruptured uterus with escape of placenta into the peritoneal cavity was now manifest, but the patient's condition at this time did not warrant further surgical interference. Following this procedure the peritoneal symptoms subsided and the general condition of the patient improved.

On the next day, May 21, a laparotomy was performed. On opening the abdomen a rent in the lateral uterine wall, about 10 cm. in length, extending from the left cornu in a vertical direction downward to the level of the internal os, was found. The placenta was dark in color, very spongy, almost liquid in consistency. The right side of the pelvis was completely plastered down by exudate. The placenta was removed and the rent in the uterus exposed. The uterus itself was fixed. Hysterectomy in the presence of infection, as evidenced by the conditions previously described, was deemed not only inadvisable but disastrous. The tear in the uterus was therefore repaired by the use of doubled sutures of No. 2 chromic catgut. The approximation of the torn edges was difficult on account of the friability of the uterine wall. After closure of the tear the uterus was attached to and covered by parietal peritoneum so as to make this organ extraperitoneal. The abdomen was closed and drained. Immediately following the operation a transfusion of 400 c.c. of blood was given.

For about forty-eight hours following the operation the patient suffered considerably from abdominal distension. The temperature hovered continuously between 101° and 102° for twelve days during which period there was profuse purulent discharge from the abdominal wound as well as from the vagina. Her general condition, however, continued to manifest a steady improvement; and, on the twenty-ninth day after operation, the patient was allowed out of bed. On the twenty-third of June a vaginal examination disclosed the posterior colpotomy wound almost healed but a mass was palpable in the culdesac.

After dilation of the posterior colpotomy wound considerable pus and a strip of iodoform gauze escaped. The patient was discharged on the fifty-second day after operation. Examination at this time revealed a good general condition; abdominal wound well healed, except for a small granulating area at its lower angle; and the posterior colpotomy wound almost entirely healed with some induration around it. The uterus was involved, held up high and to the left, with no palpable exudate present. A blood count at this time showed 5,200,000 R.B.C.; 65 per cent HGB.; 12,000 W.B.C.; 64 polys; and 36 lymphocytes.

The interesting features in this case are: first, the cause of rupture which I was unable to establish; second, the escape of the placenta through the uterine rent into the peritoneal cavity and its retention for five days; and third, the conservative operative procedure.

An important causative factor in the perforation of the uterus in the early stages of pregnancy is the malposition of the organ, the uterus being usually in retroflexion. A sound or dilator is introduced and passed through the anterior wall of the uterus. The operator believing that he has entered the cavity of the uterus follows this by the introduction of a placental forceps or a curette and in his attempt to extract what he believes to be the uterine contents, delivers instead intraabdominal contents, usually small intestine or omentum.

The causative factors of full-term injuries of the uterus are numerous and varied. In the cases of this series the causative factors have already been described.

The treatment of uterine injuries may be briefly stated as prophylactic and curative. The prophylactic treatment consists in the proper determination of the correct position of the uterus and the exercise of careful instrumentation. When a uterine sound has passed to a greater distance than the supposed stage of the pregnancy one should at once suspect a perforation. In the full-term pregnant uterus all intra-

uterine manipulations must be carefully executed; the use of pituitrin must be well indicated.

The surgical treatment should be instituted as quickly as possible after the occurrence of the calamity, and as the greatest danger is peritoneal infection, the cases operated on within twelve hours after injury has occurred have the best chance for recovery.

The surgical treatment should consist of the repair of all intestinal or omental injuries. Conservation and not the extirpation of the uterus and appendages should be the rule. I believe that I have demonstrated at least to myself that the conservative treatment of uterine injuries is not only feasible but is successful. In five of these cases in which conservative surgery was practiced not only have the patients recovered but have retained their menstrual and generative functions.

849 PARK PLACE.

(For discussion, see page 123.)

REPORT ON SEVENTY-SIX CASES OF ECTOPIC GESTATION

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IT IS only about fifty years ago that Parry¹ expressed the accepted theory of his time when he said that the accident of ectopic gestation was almost always fatal and that there were no reliable means to combat its dangers. Since that time, there is nothing in the surgical field that has shown such brilliant progress as the diagnosis and treatment of ectopic pregnancy.

Any pathologic or abnormal condition of the female genitals may be a focus or cause of this accident. In our series, 2 cases followed vaginal incision and drainage done four and five years previously. Hydrosalpinx on the opposite side was found several times and one followed a Rubin test for sterility. Williams² found evidence of inflammatory reaction in all specimens examined, and these were bilateral in all cases where both tubes were removed.

Ectopic gestation may occur during any time of the child-bearing period. Our youngest patient, who had had a child seven months previously, was nineteen years old. The oldest patient was forty-one years old.

TABLE I.—PARITY

SINGLE	I	II	III	IV	V	VI	VII
1	31	16	14	9	4	0	1

It is interesting to note that thirty-one of our series, or over 40 per cent, were primiparae.

The diagnosis of early ectopic gestation is very difficult to make. In many cases, with typical textbook symptoms, we found no extra-uterine pregnancy; and again, we found this condition when the symptoms and history suggested other disorders.

Many patients have been curetted under the impression that they were suffering from an incomplete abortion which subsequently proved to be an ectopic pregnancy. Ten, or 13 per cent, of our series had been curetted (prior to admission to the hospital) from six days to eight weeks before the true condition was recognized.

TABLE II.—CASES CURETTED FOR SUPPOSED MISCARRIAGE

NUMBER	1	2	3	4	5	6	7	8	9	10
No. of days before true diagnosis	6	9	10	11	12	14	19	28	42	56

Our experience coincides with that of Oastler;³ namely, that in many cases tenderness of the mass is out of all proportion to its size and density, and that traction on the cervix or active manipulation of the uterus generally aggravates the pain and tenderness. These symptoms may disappear for days or weeks and recur with exacerbations until some marked changes take place. Nine of our patients gave the above history.

At the beginning of rupture or tubal abortion there may be symptoms of an acute abdomen of moderate severity without any definite findings in the adnexal regions. There may be a slight elevation of temperature, pulse rate, and leucocytosis, with very little change in the sedimentation time. The hemoglobin or the number of red blood cells may not be affected.

When a massive hemorrhage suddenly occurs, signs of shock and collapse, distention of the abdomen, and at times unconsciousness are present. The peritoneal reaction, so-called "peritoneal kick," is usually present. Contrary to Schumann¹ and DeLee,⁴ we found shifting dullness in at least 7 of our 76 cases. Cullen's sign, i.e., dark discoloration at the umbilicus was noted three times. Twelve patients were in shock on admission to the hospital.

There is another type in which there are slow repeated attacks of pain and internal bleeding, and a gradual increasing anemia and weakness. Vaginal examination shows the pelvis filled by an indefinite tender mass, which seems to encompass the pelvic organs. Jaundice, nephritis, and fever are not unusual complications at this stage.

The following terms were used by the patients to describe the types of pain that they suffered: sharp, bearing down, tearing-like pain; intermittent labor-like, dull ache, severe cramp, extreme agony, gas-like pains, pressure sensation, feeling of weight in the rectum, bladder, or back. These pains often occur during sleep, while walking,

riding, during intercourse, or after eating. They frequently radiate to the epigastrium, shoulder, thorax, or to the back.

Pain in the bladder region, frequent micturition, vaginal and rectal discomfort, or pain radiating down the thighs is not uncommon. Constipation, obstipation or diarrhea, and rectal tenesmas were also noted.

The right side was affected in 45 and the left in 31 cases. Occasionally the uterine artery on the affected side was more easily palpated than on the opposite side, but we do not feel that is a pathognomonic sign.

Thirty-nine of our series (i.e., 51 per cent) complained of vaginal bleeding, which varied from a scant, intermittent "show" to profuse bleeding (often clotted) which lasted several weeks. This is a very significant sign and frequently leads to a mistaken diagnosis of an incomplete or a threatened abortion.

Ectopic pregnancy must be differentiated from: (1) early uterine pregnancy, with an enlarged corpus luteum of the ovary; (2) threatened miscarriage; (3) rupture of a graafian follicle, with internal hemorrhage;⁵ (4) torsion of a tube and ovary; (5) torsion of an early pregnant uterus, complicated by soft fibroids and recent omental adhesions (author's case); (6) ovarian cyst with twisted pedicle; (7) acute or subacute salpingitis; (8) hydrosalpinx; (9) acute appendicitis; (10) rupture of gastric or duodenal ulcer, and from (11) ureteral or renal colic.

There are two outstanding features in the diagnosis of extrauterine pregnancy.

1. Pain, as described above. This combined with the history of a possible pregnancy, an indefinite fullness and tenderness in the pelvis, combined with

2. A bloody "show" which does not appear at the regular or expected menstrual period, should be suggestive of extrauterine pregnancy. The presence of clotted particles of blood on vaginal puncture is indicative of pelvic hemorrhage so frequently associated with ectopic pregnancy and may help to decide the diagnosis.

As previously stated, the diagnosis of an unruptured or partially ruptured ectopic pregnancy is at times very difficult to make, but fortunately the treatment for all conditions with which it might be confused is an operation. The only exception would be an acute salpingitis.

The advance in the treatment of ectopic gestation has reduced the mortality from 85 to about 5 per cent and has markedly decreased the morbidity, chronic invalidism, and the period of convalescence. There were 4 deaths in our series; 1 from peritonitis, 1 from cardiac failure with pulmonary edema, 1 from shock, and 1 patient, who had suppurating salpingo-oophoritis at the same time, died of Streptococcus hemolyticus peritonitis. Most of the patients leave the hospital

from two to three weeks after the operation with no worse effects than is usual with operative cases. These remarkable results can be attributed to prompt operative procedure and to the wonderful effect of blood transfusion plus the routine treatment of shock. Thirteen patients were transfused just before or during the operation and 4 were transfused immediately after.

If the patient is in a dangerous condition, only the affected tube is removed; otherwise we have been in the habit of taking care of all lesions present. We have performed a number of curettements in order that the decidual reaction in the cases might be studied by Dr. B. S. Kline, pathologist of Mt. Sinai Hospital. There has always been a marked difference of opinion by various authorities as to the diagnostic value of the decidual reaction in uterine scrapings. I believe that the conclusions which he has drawn and presented in a companion paper deserve careful consideration.

We do not irrigate the abdomen after the operation, but we do remove most of the blood clots. Drainage is seldom used, as the peritoneum can usually take care of the remaining blood and serum. If an accumulation forms in the culdesac, it is very often absorbed in a short time. If it becomes infected, it is then well localized and circumscribed and may be readily evacuated by vaginal incision and drainage.

After operation all patients are kept on either strict or modified peritonitis treatment for from twenty-four to forty-eight hours, depending on their condition. This treatment consists of the use of Fowler's position, saline infusions (1500 to 3000 c.c. per day), occasionally 500 c.c. of 5 to 10 per cent glucose solution intravenously, hot stupes to the abdomen, and enough morphine-sulphate by hypodermic injection to keep the patient comfortable and to hold the respirations below 20 per minute.

The following complications occurred in our series: 2 cases of each of the following: parotitis, phlebitis, peritonitis; 1 each of edema of the lungs, intestinal obstruction, pelvic abscess; and one case of acute mania.

CONCLUSIONS

1. Ectopic pregnancy may occur at any time in the childbearing age.
2. There is a greater percentage of ectopic gestation in primiparae than is usually suspected.
3. Pain, as described above, is the most constant and significant symptom.
4. Irregular and prolonged bleeding, suggesting a threatened abortion, often occurs, in contrast to the infrequent occurrence of vaginal bleeding in early uterine pregnancy.

5. Immediate operation, except in cases of infection, plus transfusion and careful after-care, is the safest and best method of treatment.

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7016 EUCLID AVE.

THE FETAL MORTALITY IN BREECH PRESENTATIONS. IS PROPHYLACTIC EXTERNAL VERSION ADVISABLE?*

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The fetal mortality in breech presentation is variously estimated.

DeLee¹ says that it is between 6 and 15 per cent, and states that with proper care it should not be over 5 per cent in uncomplicated cases. Bumm² puts the figure at 15 per cent. According to Williams³ it is between 10 and 15 per cent in primiparae, with a lower rate in multiparae. Polak⁴ says that it is at least 10 per cent in primiparae, but claims that with skilled assistance it should be almost as low as in vertex presentations. Similar figures are given by Shears,⁵ Edgar-Vaux,⁶ and Tweedy, Wrench and Solomons.⁷ Wallich, of Paris,⁸ quotes statistics collected by Hegar, which show a 40 per cent fetal mortality in rural practice; in the Clinie Baudelocque, on the contrary, it is given as 3.5 per cent, while in the Clinie Tarnier, the figure for frank breech cases is given as 7 per cent. Irving and Goethals,⁹ in a series of 235 breech deliveries occurring in the Boston Lying-In Hospital over a period of fourteen years, found the fetal mortality to be 9.78 per cent (12.7 per cent for the primiparae and 7.8 per cent for the multiparae). Pierson,¹⁰ in 122 cases at the Sloane Hospital for Women, reports the fetal mortality as 12 per cent. Gibberd,¹¹ however, thinks that the figures usually quoted are much too low, at any rate, as far as average medical practice is concerned. He reports 135 uncomplicated breech cases delivered in the Guy's Hospital District. He does not state whether these were hospital or home deliveries, but one would infer the latter to be the case. Of these patients, 29 were primiparae, with a primary fetal mortality of 28 per cent and an additional neonatal mortality of 3.5 per cent, and 106 were multiparae with a primary fetal mortality of 14 per cent and a neonatal death rate of 1 per cent in addition. He states that this is to be considered as an exceptionally unfortunate series if the generally accepted figures are correct, or else that these figures are much too low. In substantiation of the latter view, he quotes figures collected by him from six different hospitals, which showed, in 136 uncomplicated cases, a primary fetal mortality of 26 per cent, and an additional neonatal mortality of 6 per cent.

*Read before the New Orleans Gynecological and Obstetrical Society. Meeting of April 19, 1928.

It is generally stated that the chief dangers to the fetus are asphyxia and compression of the cord; hence, the time honored maximum of eight minutes from the birth of the umbilicus to the delivery of the head.

The more recent texts do not insist so strongly on this point, though Tweedy, Wrench, and Solomons⁷ state that if the cord circulation stops for four minutes the child will probably die. Holland,¹² on the contrary, feels that the fetus is not any the worse for fifteen or twenty minutes of cord compression. Potter, as is well known, extends the limit of safety to fifteen or more minutes, and stated to me that in one instance he had delivered a live baby twenty-six minutes after the cord pulsation had ceased during the performance of a version. It is now a matter of general knowledge that many of the fetal deaths occurring during or shortly after breech delivery are due to birth injuries and not to anoxemia; Holland, for instance, states that tears of the tentorium and cerebral hemorrhage are almost constantly found in dead babies delivered by the breech. Pierson, in his review of 122 primary breech deliveries of viable babies at the Sloane Hospital for Women, reports 18 fetal deaths (12 per cent). In 87 viable babies delivered by version, the fetal mortality was 18 (26 per cent). In 17, or 47 per cent, of these 36 fetuses, spinal cord hemorrhage was found at autopsy, while 4 showed partial or complete rupture of the spinal cord. In 14, or 38 per cent, one or more fractured vertebrae were found, and in 9, or 25 per cent, cerebral hemorrhage, varying in degree from moderate to severe, was noted. Pierson quotes Brown as stating that cerebral hemorrhage is ten times more likely to occur in breech delivery than in delivery by the vertex, and that hemorrhage into the adrenals is twenty-two times more frequent in the former. One of the fetal deaths reported in this paper was due to a rupture of the left adrenal.

The management of the delivery is generally considered to be responsible for these birth injuries rather than the presentation itself. Many feel that rigid adherence to the eight-minute rule, with hasty and unskillful manipulations, not infrequently leads to fetal death. This is especially stressed by Holland.

Pierson states that two errors in judgment stand out in the series reported by him: (a) hurried conduct of the delivery, or, as he well phrases it, frantic haste rather than deliberate skill; (b) misjudgment of the pelvis, as exemplified by the fact that 50 per cent of the pelvis in the version cases and 6 per cent in the primary breech series were abnormal. He also stresses two errors in technic: (a) failure during delivery to accommodate the long axis of the child to the pelvis axis, thereby causing dangerous angulation; (b) failure to accommodate the long diameters of body, shoulders, and head to the long diameters of the pelvis, resulting in too much traction and in undue suprapubic pressure.

It appears then, that some revision in the technic heretofore employed in the management of breech delivery is indicated, and this tendency is noted in the recent literature as well as in the recent revisions of the various textbooks on obstetrics.

Holland thinks that it is entirely wrong to hasten delivery of the aftercoming head, but that we should deliver it gently and gradually. He also lays great emphasis on the value of episiotomy as a means of saving the fetal head from excessive stress. Meeker and Bonar¹³ state that sacral anesthesia is of great value

in breech presentations on account of the marked relaxation of the perineum thus obtained. Wallich and other writers speak enthusiastically of the dilatation of the vagina by hydrostatic bags. A preliminary "ironing out" of the vagina is recommended by Potter and others. The various texts consulted all recommend expectant treatment during the delivery, without undue haste, together with the avoidance of traction as much as possible. True, Shears states that as soon as the breech appears at the vulva, the delivery is to be hastened as much as possible, and Tweedy and his coauthors state that the child's life depends on the speed and skill of the delivery, but we may safely assume that these writers are referring to skillful expedition and are not advocating rough maneuvers. Some writers, notably DeLee and Edgar-Vaux, recommend forceps to the aftercoming head in difficult cases. Irving and Goethals, at the Boston Lying-In Hospital, tested out the policy of delivery as soon as the cervix was fully dilated. Their method was as follows: surgical anesthesia, the bringing down of one foot or both feet, if possible (using the Pinard maneuver in frank breech cases), extraction of the arms anteriorly, and delivery of the head either by suprapubic pressure combined with the Mauriceau method or by the use of forceps in an occasional instance. Thirty cases were managed in this manner in the course of a year; thirteen were primiparae and seventeen were multiparae. One baby was lost in each series, giving a total fetal mortality of 6.6 per cent (7.7 per cent in the primiparae and 5.8 per cent in the multiparae). The rate for several years preceding this test was 11 per cent. The authors state that this method has been followed in the main in this hospital since these observations were made, with a definite lowering of the fetal mortality.

Even the lowest of these mortality figures for breech deliveries, however, is much higher than the fetal death rate in vertex presentations, hence we find that prophylactic external version has long been recommended by many authorities, and is attracting renewed interest at present.

Gibberd, in view of the high fetal mortality in his series, heartily recommends the method and reports his experience with it. In 232 cases, he failed 58 times. Of these 17 babies later turned spontaneously, in 18 instances no further attempt was made, while in 18 others a second attempt was successful in eight patients. The babies which were turned sustained a primary fetal mortality of 2 per cent and a neonatal death rate of 1.4 per cent. The author feels that the optimum time for the performance of the version is between the thirty-second and the thirty-sixth week. If tried earlier, the position is especially liable to recur, while after the thirty-sixth week the operation becomes increasingly difficult the nearer we approach term. It is well to note that no case of prolapsed cord or of placental separation was encountered in the patients upon whom this version was performed. Ryder¹⁴ reports a similar series, consisting of 49 patients under observation before the onset of labor, and three who were not seen until labor had begun. Of the 49, external version was performed on 29 patients; of these, one recurred and was delivered by the breech, one was delivered by cesarean section, and the other 27 were delivered as vertex presentations. The attempt at external version was unsuccessful in four instances, and in the 16 patients remaining, for various reasons, it was not tried. All these 49 babies lived. In the three patients seen after the onset of labor, the version was successfully performed in one instance. In all the versions on primiparae the new position was permanent, but the breech presentation recurred in several of the multiparae.

More recently, Bartholomew¹⁵ reported his results with external version in a personal series of 54 breech presentations. In 13 cases the attempts were not successful, but in 6 of these the baby later turned spontaneously before term was reached, so that only 7 of the children were delivered by the breech. In his last 37 cases, after some experience was gained, the version was successful in 35. In one of the unsuccessful attempts the turning was probably tried too early (at the seventh month), and in the other patient a dense area of scar tissue in the lower right abdominal quadrant (following an operation for suppurative appendicitis) greatly hampered the operator in his manipulations. Experience of the writer and others showed that there is no advantage in trying to retain the baby in the corrected position by pads and bandages. In this series, no babies were lost, nor did premature separation of the placenta or premature rupture of the membranes occur. He agrees that the most favorable time is during the eighth month. If the first attempt fails, one or more additional trials may be in order.

The technic of this procedure is simple. The patient's bladder and rectum should be empty. The dorsal position is employed, with the lower extremities flexed to relax the abdominal muscles. Some writers prefer the Trendelenberg posture. At times, especially in primiparae, an anesthetic, preferably ether, is necessary in order to secure the necessary relaxation. The breech is raised from the pelvis with one hand, and is carried toward the iliac fossa on the side to which the baby's back is pointing, while the head is brought down on the opposite side by the other hand, thus maintaining the body in a position of flexion. In some instances this procedure will fail and version in the opposite direction will be successful. Gibberd, Reyder, and Bartholomew all state that no untoward results were noted in their series, such as premature separation of the placenta, prolapse of the cord, rupture of the membranes, etc. However, a case of fetal death following external version has recently been reported by Fruhinsholz,¹⁶ who thought that the fatality was due to pressure of the fetal head against the placental vessels at the insertion of the cord. DeLee,¹⁷ in commenting on this paper, stated that he knew of two deaths following this procedure. Hence, it is essential that the utmost gentleness be employed, and that force be not employed to overcome resistance, if encountered.

In an attempt to determine the local fetal mortality in breech presentations, we have analyzed the cases cared for during the past few years in the Charity Hospital and the Touro Infirmary. Patients with babies weighing less than five pounds have been eliminated, as a fetal death from prematurity cannot in fairness be ascribed to the presentation or to the method of delivery, and conversely a successful delivery of a premature infant is no testimony as to the accoucher's skill. Patients delivered of macerated babies have likewise been eliminated, as well as cases of multiple pregnancy. In the Charity Hospital we studied the records of 78 patients delivered in the white obstetric service. Thirty-one were primiparae, with a fetal death rate of two, or 6.4 per cent, and 47 were multiparae, with a fetal mortality of 6, or 12.8 per cent. At the Touro Infirmary we reviewed the records of 80 cases, 33 being multiparae and 47 primiparae. There were four fetal deaths in each series, giving a fetal mortality of 9.3 per cent for the latter and 12.12 per cent for the former, with a rate of 10 per cent for the series as a whole. Combining the two

series, we find a total of 158 cases, with 16 fetal deaths, or 10.12 per cent; in the group comprising the primiparae there were 78 cases, with six fetal deaths, or 7.7 per cent, while in the second group of 80 multiparae there were ten fetal deaths, or 12.5 per cent.

These figures are somewhat better than we had anticipated, especially as regards the work at the Charity Hospital, where most of the cases under consideration were admitted in labor, had had no prenatal care, and in some instances had been sent in because of the inability of the attendant to accomplish delivery in the home. The results may be due to the fact that we have insisted that breech cases are not easy, and with few exceptions the patients have been delivered under the direct supervision of a member of the visiting staff, or by the staff member personally. The Touro series consists of two groups of cases, private patients and patients admitted from the free clinic. Some of the former were cared for by specialists, some by general practitioners, some by general surgeons. The clinic cases were delivered by the members of the obstetric staff of the clinic, or by the resident staff under their direct supervision. The outstanding feature of both series, as well as could be ascertained from the records, was that the majority of the patients, especially the primiparae, were delivered under anesthesia by some form or modification of breech extraction. It appears that the policy of leaving the case almost entirely to nature was not popular. It is interesting to note that in both series the fetal mortality was lower in the primiparae than in the multiparae. This is probably due to the increased weight of the dead babies born of the multiparae; seven of these ten were weighed, and the average was found to be 8 pounds, 14 ounces, with three weighing 10 pounds or more. The dead babies in the series of primiparae averaged 7 pounds, 10 ounces in weight ($1\frac{1}{4}$ pounds less than in the multiparae), and the largest one weighed 9 pounds, 13 ounces.

These 16 fetal deaths, studied in an effort to discover the causes of the fatalities, give us the following information. In the primiparae, one baby, weight $6\frac{2}{3}$ pounds, was born dead, after extraction under anesthesia. The notes stated that the heart tones were heard shortly before the onset of labor, but no further observations as to the heart tones were recorded. The other 5 babies died at periods varying from three to five days after delivery. One baby was subjected to autopsy, and intracranial hemorrhage was found. Another, born after a very difficult extraction, with futile attempts at forceps extraction of the after-coming head, died on the fifth day, with fracture of the frontal and occipital bones (confirmed by radiologic examination), and hemorrhagic disease of the newborn. Of the 3 other deaths, 2 were diagnosed clinically as due to hemorrhagic disease of the newborn, and 1 to cerebral hemorrhage. No autopsy was performed on

these babies. Of the 10 fetal deaths occurring in the series of 80 multiparae, two occurred in women, each of whom gave a history of stillbirth in the preceding (and only other) pregnancy. This information should have put the obstetrician on his guard. On one chart the pelvic measurements were recorded as normal, while no note as to this point was found on the other record. Another baby, weighing 10 pounds, died three days after delivery; at autopsy, the death was found to be due to hemorrhage following rupture of the left adrenal. Two other babies were dead when the patients were first seen. Two deaths were due to the great difficulty in extracting the after-coming head; in one instance there was also extension of the arms. Two others were born dead after extraction for frank breech presentation; in one instance, the baby weighing $11\frac{1}{2}$ pounds, the notes state that delivery as soon as the cervix was fully dilated would probably have saved the infant. In the tenth case, the baby, weighing 7 pounds, 5 ounces, was born precipitately, was resuscitated, and died a few hours later. No cause could be assigned, and no autopsy was obtained.

Considering these results in our local institutions, should we recommend prophylactic external version? We might remark that we have attempted it only a few times with an occasional success, as most of the patients delivered by us or under our supervision were emergency cases at the Charity Hospital, and were not seen until they were admitted in labor. However, it appears to us, after this review of the local situation and of the experiences of others, that it is advisable to attempt to turn these babies by the method above outlined, even though the fetal mortality in this series in no way approaches the figures given by Gibberd. It would seem that external version would be especially indicated in the work of the occasional accoucheur, whose fetal mortality in breech cases will naturally be higher than that of the specialist, particularly if the delivery is to be conducted in the home without adequate facilities. Under these very circumstances, however, it is least likely to be tried, chiefly because, on account of faulty prenatal care, the diagnosis is frequently not made sufficiently early. Hence it would appear that in our teaching we should continue to stress early obstetric diagnosis, and should in addition train our students in the performance of prophylactic external version.

To recapitulate, then, we would recommend an attempt to turn the baby by external manipulations between the thirty-second and thirty-sixth weeks, when the diagnosis of breech presentation is made that early. If the version fails or if the patient is not seen until labor has begun, we feel that the best results are obtained by breech extraction under surgical anesthesia with ether. In our opinion, this is best begun in the case of a full breech when the buttocks begin to emerge from the vulva, while in frank breech and in footling cases (on ac-

count of the danger of prolapsed cord) it is well to undertake it as soon as the cervix is fully dilated. Colpeuryesis by a hydrostatic bag or the ironing out of the vagina will be of great assistance, and episiotomy is wise in most primiparae. Forceps to the after-coming head will at times be a lifesaving procedure.

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(For discussion, see page 130.)

ANEMIA IN PREGNANCY*

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WE ARE constantly endeavoring in our practice of prenatal care to give the pregnant woman advice that will be of benefit to her in every way. There is some tendency, however, to give the subject of toxemia the greater attention, neglecting many other things of equal importance. The problem of anemia in pregnancy has been very inadequately treated in the literature. Of the little which has been written the greater part deals with the so-called pernicious anemia of late pregnancy and the puerperium. Only ninety references could be found relative to the subject and all but ten of these dealt with this variety.

Walter Channing was the first to describe the pernicious anemia of pregnancy in 1842. Most of the cases recorded are found in the German and French literature. Esch reviewed the German literature exhaustively in his articles covering the years 1911 to 1927. Schmidt of Detroit has made a special study of the subject. Larrabee and Minot (Boston), Rowland (Cleveland), Kerwin (St. Louis), G. H. Schneider, Oettingen and Alder of Germany have also added to the knowledge of the condition.

The short study herein presented does not include any cases of so-called pernicious anemia of pregnancy but deals entirely with the so-called physiologic anemia. Gram of Denmark, Kerwin and Collins

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of St. Louis, Thompson of Johns Hopkins, and Poul Kühnel of Germany are some of the most important contributors to this subject. Kühnel's article covers a very thorough study of the blood in fifteen normal pregnant women, recording their blood findings every two weeks during pregnancy and also at intervals of one to three months for one year after delivery.

It has been shown also that we not only have the common physiologic anemia and the pernicious-like anemia of pregnancy but that a certain number of cases of true pernicious anemia start with pregnancy. In Cabot's 1200 cases of pernicious anemia 434 were in women and 35 of these started with pregnancy.

Etiology.—From the literature it would seem that anemia during pregnancy is the result of the destruction of maternal blood cells by the chorion, presumably to allow the blood elements to be taken up into the fetal circulation. Some evidence of this destruction can be found in the liver and spleen and by an increased amount of iron in the urine. Strahl, Bounet, Kolster, Hoffbauer, Wychel and Payer have all demonstrated absorption of hemoglobin and erythrocytes by the ectoderm cells of the chorion.

R. Freund, Mohr, Polano and Rucher have all found lipoid substances in the placenta. Mohr and Freund assume that these hemolyzers normally produce solution of maternal erythrocytes in the placenta.

It seems logical to assume that the blood-forming organs of the body attempt to replace the blood destroyed and if they fail to respond properly anemia will result.

Alder believes that the so-called pernicious anemia of pregnancy occurs only on the basis of a primarily injured, poorly functioning bone marrow. Esch, however, studied carefully the reports of forty-eight cases and in only 35 per cent could he assume the presence of a functionally injured bone marrow.

Diagnosis.—The diagnosis of anemia is, of course, made only by examination of the blood. Many pregnant women, having a well-developed anemia, show no pallor. Even where pallor is evident a blood count should be made because pallor and anemia are not always associated.

The pernicious-like type of anemia occurs only in the last few months of pregnancy or during the early puerperium. Over two hundred cases have been reported. They have all apparently been cases that have had little or no prenatal care. Esch compiled 23 cases with a mortality of 70 per cent. Schevlov compiled 52 cases with a mortality of 65 per cent. Seitz reported 43 cases with a mortality of 50 per cent. Aubertin reported 53 cases and stated that recovery was very rare. There is extreme pallor with a yellow tint to the skin, extreme weakness, no loss of weight, but instead, edema, diarrhea with colorless stools, low fever, vomiting, sore mouth, achlorhydria

and the blood picture is almost identical with true pernicious anemia. Labor is generally premature, of short duration, with very little pain and scant bleeding. Both Heim and Offergeld state that the baby is free from anemia while in true pernicious anemia it never escapes.

Report of Blood Examinations.—The blood examinations here presented were all done on my private cases but do not constitute a deliberate, systematic study of the subject of anemia. The figures represent a compilation of 364 routine blood examinations on 228 consecutive cases delivered over a period of fourteen months ending November 9, 1927. Sixty-eight of the 228 cases had not had an examination of the blood during pregnancy so that only 160 cases are recorded. Sixty-two cases had only one examination, 46 had two examinations and 53 cases were examined three or more times.

Eighty-seven patients were examined during the first twelve weeks of pregnancy. The average hemoglobin of these 87 examinations was 72.5 per cent. The average red cell count was 3,630,000.

Seventy-seven patients were examined between the twelfth and the twenty-eighth week of pregnancy. The average of 84 hemoglobin estimations was 70 per cent. The average of sixty-six red cell counts was 3,560,000.

Sixty-nine patients were examined between the twenty-eighth week and term. Seventy-two hemoglobin estimations gave an average of 71 per cent. Forty-one red cell counts gave an average of 3,820,000.

It has been the general belief that anemia was more apt to occur in early pregnancy with a gradual rise to near normal at the ninth month. Such a statement was made by Osler based on a study by W. L. Thompson in William's Clinic at Johns Hopkins. The above findings do not bear this out. The average count was no better in the last trimester than during the first or second notwithstanding the treatment which will be discussed later. Moreover, some of the most severe cases of anemia developed during the last trimester. Kerwin and Collins made thirty estimations of hemoglobin in the first trimester with an average of 83 per cent, eighty-eight in the second trimester with an average of 83 per cent, and eighty-six in the third trimester with an average of 82 per cent. This also shows a uniform hemoglobin for the three trimesters, although relatively high. H. C. Gram records 58 examinations during pregnancy with an average hemoglobin of 71 per cent for the first trimester, 72 for the second, and 79 for the third. Kühnel, in recording the study of 15 pregnant women where examination was made every two weeks, says there was a progressive anemia until the sixteenth to the twenty-second week, that this low mark was stationary until the thirtieth to the thirty-second week when improvement occurred and the curve reached its height at the thirty-fourth week. He also stated that the hemoglobin curve made a more pronounced drop than the erythrocyte curve.

Taking the entire 243 hemoglobin estimations made by me during all months of pregnancy, the average was found to be 71 per cent. The average red cell count taken from 194 examinations under the same conditions was found to be 3,660,000.

A letter was recently sent out to 75 of these patients asking them to come into the office for blood examinations while they were not pregnant and 39 responded. They were all over three and one-half months away from delivery and 33 out of the 39 were over five months from delivery. The average hemoglobin was 85 per cent and the average red cell count was 4,710,000.

The records of 33 examinations were found that had been made during the first twelve postpartum days. The average hemoglobin was 80 per cent and the average red cell count was 4,450,000. Three cases of postpartum hemorrhage were omitted from this group.

Twenty-five examinations were made at the eighth week postpartum when it is customary to make a physical examination. The average hemoglobin of these 25 examinations was 81 per cent and the average red cell count was 4,440,000.

Alder examined 11 patients during pregnancy and again during the puerperium. In pregnancy the average hemoglobin was 50 per cent and the average red cell count was 3,680,000. In the puerperium the average hemoglobin was 73 per cent and the average red cell count was 4,430,000. Kühnel's records show a hemoglobin and red cell count on the tenth postpartum day almost as high as the sixth month after delivery. The findings of these two authors and the figures given above all correspond and show that the anemia of pregnancy disappears very shortly after delivery.

Treatment.—The majority of the patients in this group of 160 who showed a tendency to become anemic were given treatment. No rule was followed but generally if the hemoglobin dropped below 70 per cent a preparation of iron and arsenic was given by mouth three times a day with meals and diet containing considerable iron was prescribed. If no improvement occurred after a month or more of this treatment they were given a series of exposures with the ultraviolet light at two-day intervals and at the time of each treatment iron was administered with a hypodermic syringe, generally intramuscularly. Twenty-seven out of 41 cases that had to be treated in this manner showed satisfactory improvement. Four of these patients became severely anemic again, however, before delivery occurred and were again given the same treatment and with the same satisfactory results. Four of the 41 remained the same, three became more anemic in spite of this treatment and no records were available on the results in seven. The three cases that did not respond to treatment were not severe. All three had a hemoglobin between 60 per cent and 70 per cent.

The most effective treatment of the pernicious anemia of pregnancy seems to be repeated injections of small amounts of whole blood, or repeated, small transfusions. Claiborne Smith had very good success in eight cases with the administration of dilute hydrochloric acid. Aubertin who reported 53 cases stated that recovery, though rare, occurred only where the uterus was empty. Only a few authors, however, recommend induction of labor.

CONCLUSIONS

1. The majority of women, when pregnant, have a lower hemoglobin and fewer erythrocytes per cubic millimeter.
2. This anemia condition will, in the majority of cases, disappear within two weeks after delivery.
3. The use of ultraviolet light together with the intramuscular injection of iron will help prevent severe anemia in pregnant women.

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SOME PHYSIOLOGIC ASPECTS OF ECLAMPTIC TOXEMIA*

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OF THE complications of pregnancy, none seem to have been as extensively studied or written about as the toxemia occurring usually late in gestation. Its etiology remains unknown, but is the subject of relentless research. The treatment of choice tends to conservative management, distinctly noninterfering, with results that are most gratifying as compared to former methods, and as a consequence this mode of treatment appears to have become a fixture in our obstetric armamentarium.

Realizing that this subject has so many interesting and debatable angles, I will restrict my discussion to a consideration of this complication from the standpoint of some of its physiologic aspects adding such comments as I consider pertinent.

About seven years ago, dissatisfied with the results we were obtaining from the then generally accepted treatment of eclampsia, we began to apply ourselves to the study of these cases, prenatal, natal and postnatal, and made several observations, which not entirely new, were nevertheless very interesting.

It was noted that this toxemia occurred more frequently in the negro than in the white; in the latter, considered from the economic standpoint, oftener among the lower than the upper classes. Individuals of the stout and plethoric types were more prone to its development. Most significant was the fact that this complication occurred in less than 10 per cent of the maternity cases that were properly supervised during the prenatal period, and that when such symptoms did appear they were readily amenable to corrective and protective measures. Equally significant was the fact that whenever this toxemia became a serious complication it always responded to the same protective, corrective, and eliminative measures. We, therefore, seemed to be dealing with an entity whose cause is unknown, and which can be eliminated or controlled by a plan of treatment which as a whole sought to restore and equalize the several body functions.

It is a notorious fact that the average individual consumes a diet excessively high in protein, and the usual intake is twice as much as the body requirements. Poor hygiene, insufficient exercise, low fluid ingestion and improper diet all tend to constipation and the retention and concentration in the body of materials which first overload, and

*Read before the New Orleans Gynecological and Obstetrical Society. Meeting of April 19, 1928.

tax the various organs in a mechanical way, and finally furnish an additional burden in the form of toxic products or by-products with the resultant, inevitable breakdown of function.

These observations among others determined us to adopt the conservative treatment of eclampsia as a routine and this course was later followed by other obstetric services in the Charity Hospital.

Since then, additional observations have been made, based on the belief that the liver was the key to the solution of the question, and on the fact that it was the principal seat of abnormal postmortem finding, and because it seemed possible that the occurrence of eclampsia remained unexplained rather than undiscovered.

The changes incident to pregnancy tend to aggravate faulty personal habits, and if permitted to go uncorrected the patient comes to us with one or more symptoms of what we recognize as an impending toxemia.

The early picture then points more to a disturbance of physiology rather than to pathology. It is interesting here to review some aspects of the physiology of pregnancy, especially because in view of the common association of a high protein diet with constipation in the pregnant woman it appears that one or both may be the initial factor in the development of this toxemia. It is well to remember that the general metabolism shows a marked improvement during pregnancy, and that the katabolic processes are just as active as the anabolic. The maternal organs are called upon to take care of an added metabolism besides their own, the burden increasing with the advancement of pregnancy.

The liver, one of the organs prominently affected by this change, has several important functions: The elaboration and excretion of bile, the production of starch (glycogen) and sugar (glucose), the formation of urea, and finally, in my belief the most important, the conjugation of products of protein putrefaction.

This latter function converts the toxic products of the putrefaction of proteins into nontoxic compounds. Intestinal bacteria have a two-fold activity, fermentative and decompositive, and when the latter action on proteins is exaggerated it becomes a putrefactive process and certain toxic substances are elaborated; namely, acetic and lactic acids, and the aromatic substances, indol and skatol, cresol and phenol. These compounds are formed in the intestines and are absorbed and carried by the blood of the portal vein to the liver and in their passage through the capillaries of the liver, they are conjugated for the most part with potassium sulphate by the action of the liver cells and thus deprived of their toxicity.

Among the substances thus conjugated are indol, skatol, phenol, and cresol, and after absorption indol and skatol are oxidized to indoxyl and skatoxyl, and then combined with potassium sulphate giving rise

to potassium indoxyl and skatoxyl sulphate. All of these compounds then pass into the blood of the general circulation and finally are eliminated by the kidneys.

Potassium indoxyl sulphate is the source of the indigo-forming substance found in the urine, which is known as indican. Other compounds are likewise reduced in toxicity by the liver cells, though the method by which this is accomplished varies with the nature of the compound. The liver, therefore, presents a chemie defense against the entrance of more or less toxic agents into the blood of the general circulation.

Collectively, then, these appear to be the responsible factors: faulty hygiene, improper diet, concentration and retention due to low fluid intake and lack of exercise, constipation, intestinal putrefaction with its sequelae, an overproduction of indol, skatol, phenol, and cresol. An overwhelming of the detoxicating function of the liver with resultant necrosis from these toxins precipitates a disturbance of the remainder of hepatic function, which soon involves other organs and completes the transition to pathology. A toxemic picture of varying degrees presents itself.

The encouraging results recently reported with the administration of liver extract, a substance which seems to restore the hepatic balance, suggest that this explanation is at least tenable from the standpoint of detoxication.

Continuing our physiologic considerations, we recall that all proteins when metabolized yield a series of nitrogenous holding bodies which must be eliminated by the kidneys and the intestinal glands as well. The wear and tear of these organs will be proportional to the amount of urea and other materials which they are called upon to excrete, and if the kidneys fail to excrete these substances, some may become deposited in the tissues and give rise to certain constitutional disorders.

There is the added fact that the ammonium salts (the carbamate, carbonate, and lactate) increase in the urine when there is a destruction of the liver, and less urea can be formed. These salts are then excreted in larger quantities, which forcibly calls our attention to the physiologic embarrassment of liver and kidneys and to the interference with the important hepatic function of urea storage.

Finally, as a result of the loss of detoxicating power and of cell destruction, the glycogenolitic power of the liver is interfered with and this completes the physiologic breakdown of its function and its transition to pathology, which eventually involves the whole system.

Assuming, therefore, that these views are correct, it will be interesting to consider their relationship to the symptoms which suggest or typify eclampsia, and are grouped here in the order of their onset and severity.

Pulse Acceleration is an invariable accompaniment of this condition, most frequently the earliest sign, usually overlooked or not properly evaluated. A moderate increase in pulse rate is characteristic of a low grade of toxemia. This rate increase is seldom mentioned but is worth consideration, especially during the last trimester.

Hypertension.—This most frequent and earliest sign, in the light of our present knowledge, conclusively points to the existence of hepatic dysfunction. The satisfactory results obtained by numerous observers with liver extract in treating hypertension, actually induced Miller and Martinez of Pittsburgh to use it in cases of eclampsia, with results that are brilliant and apparently conclusive.

Reduction of blood pressure after the administration of a definite amount of this substance apparently is the result both of supplying the liver through this medium with material capable of strengthening its chemic defenses, and of restoring its detoxicating balance.

Headache is usually toxic in character, early in occurrence, and largely ascribable to the increase in blood pressure. It is of special significance when recurrent or continuous, and associated with one or more other characteristic symptoms.

Vertigo.—Like headache, vertigo is due to the toxemia plus the increased blood pressure, and suggests cerebral involvement with early edema. It frequently occurs when the toxemia has become fairly well developed, and its first appearance calls for a searching investigation.

Nausea and Vomiting.—In all probability it is toxic in origin and possibly due to a disturbance in duodenal digestion resulting from chemical changes in the biliary secretion due to a hepatitis.

Urinary Findings.—The principal anomalies consist in presence of albumin and casts. Too often this simple form of laboratory examination is omitted or neglected. The impression seems to prevail that the routine examination of a specimen once a month is sufficient for safety if albumin findings are negative. This false sense of security contributes largely to that class of cases referred to as the "fulminating type" of eclampsia.

The presence or absence of albumin, indican, intestinal putrefaction, acetone and diacetic acid, acidosis, bilirubinuria indicative of liver pathology, casts often without albumin, acute nephritis, etc., can be determined only by a complete macro- and microscopic examination of the urine.

It might be well to mention here that a differentiation between an eclamptic nephritis and a preconceptional nephritis has been made easier by the use of the bromsulphthalein dye as a test for liver function as recommended by Siegel. The dye retention is greater in eclamptic nephritis.

The test for liver function plus the urinary findings give us the laboratory line of demarcation between physiologic breakdown and its substitution by true pathology.

Edema of the Extremities.—When of toxic origin, the edema develops simultaneously with a nephritis and is soon followed by *edema of the face* which signalizes an advanced, generalized toxemia with severe renal involvement, appearing when the complication is moderately or severely advanced.

Uterine Hemorrhage is a sign not often mentioned but of great importance, especially if intermittent in type. It then suggests premature separation of the placenta as the result of toxic placental changes, and presages a premature stillbirth usually of a macerated fetus.

Dyspnea.—It is suggestive of myocardial changes and cardiac embarrassment appearing usually late in the clinical picture. It deserves more consideration than it has received in the past. The heart is the last of the organs in the eclamptic triad to succumb to the assaults of the toxemia.

Visual Disturbances.—An albuminuric retinitis or choked discs account for this symptom and, like dyspnea, develop as a rule late in the severe stage. The disturbance results from all the preceding pathologic changes with cerebral involvement and its appearance adds to the gravity of the case.

Coma, Convulsions.—More often than not they are terminal or near-terminal processes and result from uremia and intracranial pressure from cerebral edema. Broken cardiac compensation accounts for the presence of *pulmonary edema*.

One may notice that in developing and explaining the symptomatology there becomes evident a pyramiding of dysfunction, beginning in the liver, spreading to the kidneys, and finally including the heart with the inevitable result of a breakdown of function followed by the rapid development of truly pathologic conditions.

The superior mesenteric vein drains the intestinal tract all the way down to the rectum, emptying into the portal vein. Microscopically the portal venule distributes its branches through the hepatic lobule and anastomoses with the capillaries of the central vein which in turn empties into the hepatic vein.

The characteristic liver pathology in eclampsia consists in a peripheral, focal necrosis that is nearer to the portal than to the central venule. This anatomic fact suggests that toxins, carried from the intestinal canal into the liver through the portal system, cause the destruction of liver cells rather than a toxic substance formed in the liver itself and carried away through the central vein.

There are yet innumerable other possibilities. It may be that investigations of the behavior of lactic and acetic acids in the blood,

further studies of the urine, and of the manner in which the liver preserves its chemie defenses and detoxicating balance, will throw more light on the subject. The startling disappearance of certain symptoms and the rapid diminution of pathologic changes with restoration of function following the use of liver extract in sufficient amounts and at proper intervals, seem to indicate that eclampsia results primarily from a breaking down of normal liver function, the other changes being only dependent and secondary.

These reflections represent an attempt at explaining and correlating certain findings in the hope that they may form another step toward the solution of a vexatious problem. I am indebted to Dr. W. P. Gardiner, my former associate, for many of these observations.

CONCLUSIONS

1. Faulty hygiene, improper diet with constipation and intestinal putrefaction appear as predisposing factors.
2. There are indications that eclamptic toxemia primarily results from a physiologic breakdown beginning in the liver.
3. The detoxicating function of the liver appears to be disturbed first, followed by interference with other functions.
4. The transition to pathology is progressive and rapid.
5. The pyramiding of symptoms and signs results from a progressive disturbance of physiology, followed by a substitution of pathology finally involving all of the organs. Liver, kidneys and the heart become especially affected, in the order here given.
6. Pulse acceleration and intermittent vaginal bleeding are two signs which should be added to the typical picture of eclampsia.
7. From the seventh month until term the parturient woman is called upon to take care of increasing katabolic changes.
8. Protecting the patient, by careful prenatal care, against overburdening of her physiologic functions and attempting to equalize the diminished detoxicating liver function are logical demands for proper prophylaxis against eclampsia.

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(For discussion, see page 130.)

TRAUMATIC PERFORATION OF UTERUS WITH SEVERANCE OF RECTUM*

REPORT OF CASE

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THIS case is reported because of the autopsy findings and the unusual cause of death. The perforation of the wall of the uterus with pointed instruments is not an uncommon occurrence but to combine with this unfortunate accident a complete severance of the lower bowel, makes this case worthy of mention. The fact that the patient died shortly after being given a magnesium-glycerin and water enema called for laboratory investigation.

CASE REPORT

The patient, a multipara, aged thirty years, was admitted to Vanderbilt Hospital from a distant rural community. Her condition had grown steadily worse since having a spontaneous miscarriage of a five months' fetus ten hours previous to admission. The attending physician who accompanied the patient to the hospital stated that the placenta could not be expressed. He, assisted by another physician, attempted a manual removal; this failing, a pointed steel forceps was used. Before using the forceps, a cord-like structure of bluish color was seen protruding from the uterus. One physician thought it was the umbilical cord; the other thought it was intestine. It was not looped and from its ragged end exuded a brownish substance. It was removed, according to the physician.

On admission (11 P.M., Jan. 6, 1928) the patient gave the appearance of a well-nourished white woman, acutely ill, anemic, and suffering extreme pain. She had temperature of 101.6° F., pulse 115, respiration 36, B. P. 125/90. The abdomen was slightly distended and tympanitic. The slightest palpation over lower quadrants elicited complaint of pain. Patient kept her knees flexed because it was more comfortable. Uterus could not be palpated above symphysis, due to tenderness. Vaginal bleeding was moderate, and there was some edema of lower extremities. The physical examination was otherwise essentially negative. Admission laboratory report was: urine negative, R. B. C. 3,250,000; W. B. C. 15,000; hemoglobin 60 per cent, clotting time four minutes. Patient was put in Fowler's position and given morphia, 0.065 gm., pituitrin 1 c.c. and fluid extract ergot 2 c.c. every six hours.

In the forenoon of Jan. 7, patient was seen by several members of the staff. She was lying in bed quietly. The anemia was more pronounced, and abdomen markedly distended with tympany anteriorly and dullness in both flanks suggesting fluid. Abdominal tenderness was extreme. A blood culture was taken and blood typed for transfusion. Laboratory reports were: R. B. C. 3,050,000, W. B. C. 19,000, hemoglobin 55 per cent, while temperature was 102° F.; pulse 120 and respiration 44.

*Read before the Vanderbilt University Medical Society, Nashville, Tenn., April 5, 1928.

Through a bivalve speculum the placenta was seen in the cervix and easily removed without excessive bleeding. Careful examination of placenta revealed that the umbilical cord had been cut away close up to amnion and membranes torn off.

While preparations for a transfusion were being hurried, the patient was given a magnesium-glycerine and water enema to relieve the marked distention of the abdomen. Only a small amount of the fluid returned. The patient stated that she was sure she would feel much better as soon as the "gas" was passed. In less than ten minutes patient began screaming with pain in abdomen. This agony



Fig. 1.—Photograph of pelvic organs. A and B, Perforations in posterior wall of uterus, C and D, Upper end of remaining portion of rectum laid open. E and F, Torn lower end of sigmoid. G, Ovaries and tubes.

ceased in about five minutes and patient seemed to be comfortable, only to pass gradually into unconsciousness. Respiration was rapid for a few minutes and then became slower. At this moment blood pressure was 120/50 and pulse regular and of good volume. Foot of bed was elevated. In a very few minutes patient died of paralysis of the respiration, for the heart continued to beat with regularity and good volume for several minutes after respirations ceased. Death came within thirty minutes after enema was given.

Clinical diagnosis was: (1) puerperal sepsis; (2) peritonitis, acute, generalized; (3) perforation of uterus.

AUTOPSY REPORT

Upon opening the abdomen about 800 c.c. of a thin bloody fluid was found filling the peritoneal cavity. The viscera of the lower abdomen and pelvis were covered with fibrinous exudate of recent formation. The uterus was enlarged, soft, and of a deep reddish color. The anterior and lateral surfaces of uterus were smooth, but on the posterior surface were two openings situated in the midline of the organ. The upper one (Fig. 1-A.) was rounded and punched out, while the lower (Fig. 1-B.) was a transverse tear measuring 2 cm. across. These perforations were supposedly made by an instrument introduced into the uterus through the cervical canal. Beneath the uterus, as the organs lay in situ, it was found that the continuity of the sigmoid and rectum was broken by the complete severance of the rectum and apparently the removal of a portion of it.

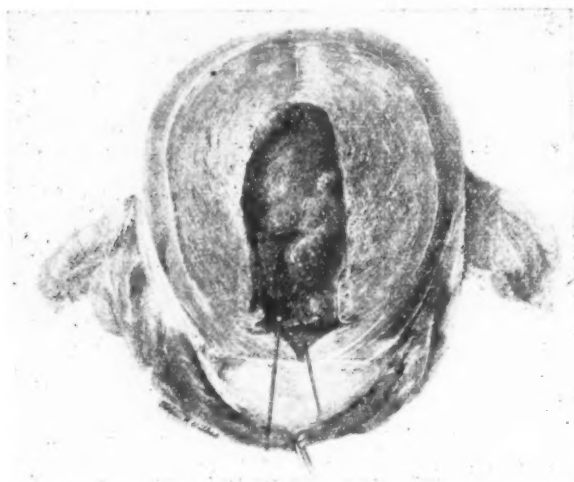


Fig. 2.—Uterus with anterior wall opened to show perforations in posterior wall.

The Pathologic Department made the following anatomic diagnoses:

1. Perforation of uterus, traumatic.
2. Tears of rectum, acute, traumatic.
3. Colitis and proctitis, acute, traumatic.
4. Peritonitis, acute, generalized.
5. Hemorrhages, subserous, multiple.
6. Endometritis, acute.
7. Pleuritis, healed.

COMMENT

It so happened that the chief of the staff was making ward rounds with the house staff at the moment when the patient made her unusual exodus and all were present to witness it. The question arose as to the immediate cause of death. No apparent reason could be advanced for respiratory paralysis, since the usual circulatory signs of shock were absent. Apparently the enema had some connection with the sudden change of the patient's condition. With knowledge of the autopsy findings it was evident that its contents had flowed into the peritoneal

cavity through the severed rectum. The enema contained magnesium sulphate, 30 c.c. (50 per cent solution), glycerin, 60 c.c., and water, 90 c.c. I conceived the idea that possibly the rapid absorption of the magnesium sulphate by the peritoneum had produced such a marked central nervous system depression that the respiratory center had been paralyzed.

Cushney¹ states that magnesium sulphate solution when given intravenously produces anesthesia resembling that of chloroform, except it results fatally with paralysis of the respiratory system. It has very little effect on the heart. He states further that when taken by mouth magnesium sulphate is so slowly absorbed from intestines that the kidneys excrete it rapidly enough to prevent its accumulation in sufficient amounts to cause any respiratory depression. Sollmann² similarly states that magnesium sulphate is a respiratory depressant, but that its action is antagonized by that of a calcium chloride solution when given intravenously. Jung and Cook³ found that they could give a rat 5 c.c. of a 1 per cent magnesium sulphate solution intraperitoneally hourly for five hours with safety, producing the usual anesthetic reaction. If, instead of the divided doses one gave 25 c.c. of the same strength in one intraperitoneal injection, the anesthesia was followed by death. The work of Lazard⁴ and his coworkers has proved the safety of intravenous magnesium sulphate treatment in eclampsia when 10 per cent solution is given in 20 c.c. amounts. Similarly, according to Dorsett⁵ patients with eclampsia have tolerated repeated intramuscular injections of small amounts of 50 per cent magnesium sulphate solution.

EXPERIMENTAL EVIDENCE

To substantiate the contention that magnesium sulphate is absorbed from the peritoneal cavity and acts as a respiratory depressant, it was decided that the contents of the magnesium-glycerin-water enema in the same proportion as used in patient be injected intraperitoneally in dogs. A dog (10 kilos) was anesthetized with ether and a kymograph rigged up to register the jugular venous pressure and the respirations. When the drum was recording everything smoothly, a mixture of magnesium sulphate, 30 c.c., glycerin, 60 c.c., and water, 90 c.c. (the same proportion and quantity of the enema given the patient) was slowly injected into the peritoneal cavity. In about five minutes the graph showed that the respirations were very rapid. This lasted only about five minutes, when they became slow and deep. The venous pressure was unchanged. Respirations ceased fifteen minutes after injection while heartbeats and venous pressure registered for a few moments. The experiment was repeated with another dog. This time only half of the above mixture was injected in 20 c.c. amounts with a few minutes between each. The animal showed the same periods of respiratory

excitement followed by depression and cessation of respirations thirty-five minutes after first injection. Venous pressure kept up for about thirty seconds and then the heart stopped suddenly. The abdomen was opened and more fluid found than was injected, suggesting that the mixture had a hygroscopic action on the peritoneum.

Next a dog was tied in a trough on his back without anesthesia. His normal respiratory rate and heartbeats per minute were noted. Half of the original mixture (90 c.c.) was injected into the peritoneal cavity. Before injection was completed the dog became restless and seemed to be having convulsive contractions of muscles of abdomen and chest. In ten minutes the dog was quiet and apparently going into a stage of anesthesia in which respiration became very rapid while heartbeats remained fairly constant. Deepest anesthesia was reached thirty minutes after injection, only the corneal reflex remaining active. Forty minutes after injection signs of returning activity were in evidence, until at ninety minutes, animal was barking and apparently conscious again. It was evident that the dog had tolerated the half dose; so the other half was given intraperitoneally. Again dog struggled for a few moments, only to pass into slow labored breathing which ceased in seven minutes after this second injection. The heartbeats stopped two minutes afterward. Peritoneal cavity was found to contain 370 c.c. of a clear fluid in excess of amount injected.

On the next animal the glycerin was eliminated from the mixture, that is, magnesium sulphate, 30 c.c. of a 50 per cent solution with 90 c.c. of water, or 120 c.c. of a 12.5 per cent solution was injected into the peritoneal cavity. No anesthesia was given. Dog was quiet throughout injection and made no noise until period of respiratory excitement came on in ten minutes. Respirations gradually slowed as anesthesia deepened, until they ceased at thirty minutes after injection. Heart continued with full beats for three and a half minutes afterward. Abdominal cavity had only 125 c.c. of fluid in excess of amount injected.

It was next decided to attempt to counteract the action of magnesium sulphate in the blood stream by intravenous injection of calcium chloride solution, since it is known to have an antagonistic action to that of magnesium sulphate. A dog was injected intraperitoneally with the same mixture (without glycerin) as used in last experiment. After three minutes of excitement respirations stopped and heart continued to beat for seven minutes. The cause of the sudden death was found when abdomen was opened. The needle had entered the liver substance, allowing some of the magnesium sulphate solution to go directly into the circulation. Another dog was more carefully injected with the same solution. It presented the same signs of all previous animals except the respirations ceased sooner than was ex-

pected (eighteen minutes after injection). Femoral vein was cut down and 10 c.c. of 2.5 per cent calcium chloride solution injected, but circulation had stopped. About 5 c.c. of the calcium chloride solution was injected directly into the heart, and it was surprising to see the circulation reestablish itself. The animal took several deep breaths (three minutes after ceasing first time) before circulation stopped. Peritoneal cavity contained only 65 c.c. in excess of injected fluid.

The above results were checked by repeating the experiment on another dog. As respirations were slowing down, 10 c.c. of 2.5 per cent calcium chloride solution was given into the femoral vein, but the heart action was sluggish; so 5 c.c. was also injected directly into the heart. Circulation was immediately reestablished and the dog breathed deep and regularly for one and a half minutes. It is probable that the large amount of magnesium sulphate already in blood stream overbalanced the action of the calcium chloride solution.

SUMMARY AND CONCLUSIONS

1. The case shows clearly the dangers of intrauterine instrumentation in attempting to remove a placenta that cannot be readily expressed.

2. The autopsy findings of traumatic perforation of wall of the uterus associated with severance of the lower bowel and removal of a part of the rectum presents a gruesome warning to all.

3. The unusual death in this case stimulated investigation into the pharmacologic action of the ingredients of a magnesium-glycerin and water enema.

4. The glycerin-magnesium sulphate combination when given intraperitoneally has a hygroscopic action on the peritoneum, in that it draws fluid into the peritoneal cavity. This action is less evident with dogs in which magnesium sulphate solution alone was used.

5. Each animal in the series died of paralysis of respiration rather than cardiac failure due to the respiratory depressive action of magnesium sulphate.

6. Calcium chloride solution given intravenously will counteract this depressive action of magnesium sulphate on the respiration.

7. The animal experimentation, while by no means complete in details, gives the laboratory evidence which was sought to support the contention that magnesium sulphate was absorbed by the peritoneum rapidly enough to produce such respiratory depression as to have caused the death of the patient.

I wish to thank Dr. Lucius E. Burch, Head of the Department of Obstetrics and Gynecology for his encouragement and keen interest in my working out this problem. Also, I thank Miss Susan H. Wilkes for the photographs and drawings of specimens.

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626 MEDICAL ARTS BUILDING.

ENDOMETRIOSIS OF AN ABDOMINAL SCAR FOLLOWING CESAREAN SECTION*

BY PERCY H. WILLIAMS, M.D., NEW YORK, N. Y.

THE case I wish to report is one of endometriosis of an abdominal scar following a second classical cesarean operation.

The patient, a woman of thirty-five, was admitted to Lenox Hill Hospital with a diagnosis of movable retroversion and an inflamed painful scar following two cesarean sections which were done respectively nine and seven years before. She admitted that the scar was somewhat changeable in color, but she had not noticed that the variation had any relation to the menstrual cycle.

Physical examination was otherwise negative except for a third degree movable retroversion which was giving her no symptoms.

The cicatrix measured 8 cm. in length and involved the umbilicus at about the junction of the upper and middle thirds. It was firm, thickened, irregular, and rather heaped up in appearance. Its surface was moist and rather sticky to the touch, she said it was constantly "perspiring." It was dull pink and had the appearance of chronically inflamed cicatricial tissue.

No hernial ring could be made out because of the brawny tissues, but a slight impulse on coughing made one suspicious of an underlying hernia.

A diagnosis of a chronically inflamed cicatrix overlying a hernia was made but a possible sarcoma could not be ruled out. Endometriosis was thought of but dismissed, because there was no history of variation of color with the phases of the menstrual cycle.

Operation took place the day after admission. The scar was excised by a narrow elliptical incision; the hernia repaired by muscular overlapping, and the excised portion sent for microscopic examination.

Convalescence was uneventful; patient left the hospital in seventeen days.

Microscopic examination of the various parts of the specimen showed diffuse involvement of the cicatrix by adenomyoma with all the characteristics of typical endometrial tissue. The tumor was poorly outlined and extended from beneath the epidermis to the peritoneal surface and laterally to the margins of the scar. The peritoneum was not involved.

The bulk of the tumor was composed of smooth muscle cells disposed in bundles running in all directions. Imbedded in this tissue were small islands of fat and epithelial tubules or cysts, either single or in groups, sometimes resting directly on the muscle but more often separated from it by zones of cellular tissue resembling the endometrial stroma. The tubules were lined with a single layer of nonciliated cuboidal or cylindrical epithelial cells. Morphologically they were identical with uterine glands. In a few tubules the epithelium was degenerated and the lumina

*Read at a meeting of the New York Obstetrical Society, May 8, 1928.

filled with granular debris. The tissue surrounding the tubules was edematous and usually infiltrated with inflammatory cells.

Whatever opinion one may hold as to the origin of the endometrial implants so ably described by Sampson,⁵ when found in other sites, this case seems undoubtedly one of transplantation to an open scar by the dragging over it of the contents of the gravid uterus during cesarean section.

Heaney,² in 1925, in describing a similar case found in the literature, reports 29 instances of endometriosis in abdominal scars. Schwartz,⁶ of St. Louis, added 2 more cases, and this case is the thirty-second.

In analyzing these 32 cases, 14, or nearly 44 per cent, followed ventral fixation. It is difficult to understand why this condition should occur so frequently after fixation when we take into consideration the comparative rarity of this operation compared to the frequency of the classical cesarean section. Is it that the sutures are often passed entirely through the muscle wall into the uterine cavity and out again through the abdominal wall, carrying grafts of endometrium with them? If so, it should warn us to pass our sutures less deeply. However, in some of these cases as the two reported by Sampson, excision or resection of the tubes was performed. Two cases, or 6.2 per cent, followed hysterectomy; whether subtotal or complete I was unable to determine, but presumably supravaginal. Three cases, or 9.3 per cent, followed unspecified pelvic operations.

Two cases, 6.2 per cent, followed appendectomy and one oophorectomy. Ten cases, or 31.2 per cent, followed either cesarean section or some operation involving the opening of the cavity of a pregnant uterus, that is, rupture of the uterus during attempted abortion, 2; hysterotomy during an operation on a pregnant uterus, 1, and cesarean section on the full-term uterus in 7.

Dr. Sampson, in kindly writing to us about this case says among other things: "I have never encountered such a case in my own practice following cesarean section. On the other hand, I have had two cases of endometriosis in the rectus muscle following fixation of the uterus to the abdominal wall. There have been cases reported of endometriosis of the abdominal scar following operation in which the uterus has not been opened and for this reason some believe that the endometriosis in these cases results from the transplantation of bits of peritoneal serosa included in the wound rather than the transplanting of uterine mucosa by the surgeon."

Nicholson³ in England and Novak⁴ in this country hold this view.

If it is difficult to understand how the müllerian mucosa can be transplanted in cases not involving the opening of the uterus or section of the tubes, it is equally difficult to understand why, if these growths result from the implantation of bits of peritoneal serosa, they have never been found except in females.

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429 PARK AVENUE.

(For discussion, see page 120.)

RECIPROCAL RELATIONS BETWEEN DISEASES OF THE ALIMENTARY AND FEMALE GENITAL SYSTEMS

BY A. J. WALSCHEID, M.D., NEW YORK, N. Y.

THE digestive system can be influenced by the female genitals and their diseases in a reflex manner through the sympathetic and parasympathetic nervous systems. This causal relationship is in evidence especially at the critical periods of puberty and the menopause, and in connection with the functions of menstruation, gestation, parturition, lactation, etc. A strong predisposition is supplied by the state of the female organs at the time, and especially at the time of the menopause, when the uterus and ovaries are undergoing regressive changes. The organs are no longer able to produce their peculiar hormones, and this deficiency disturbs the entire equilibrium of the hormonal system, which in turn is felt in the disturbed innervation of the autonomic system, manifested respectively as vagotonia or sympathetico-tonia.

Without any immediate attempt to fix the primary responsibility attention may be called to the transitory spastic states which are apt to supervene at the menopausal period in the alimentary canal from the esophagus to the colon. This spasticity may be multiple and affect different levels of the canal, and the symptom picture may not only be very complicated and varied but the frequent spastic contractions may contribute to the development of peptic ulcer. Spasticity may of course be sufficient per se to cause ileus or incomplete stasis and may also be a factor in stasis of mechanical origin. As a result, while intestinal obstruction is rare from this cause, we may readily surmise the development of general stasis and auto-intoxication.

The woman at the menopause may suffer from suppurative foci in the teeth or elsewhere in the digestive tract and the physiologic state at that epoch may possibly light up focal infection; however, the teeth should be put in order even if there is no actual evidence of focal infection.

In speaking of the disequilibrium of the hormonal system induced at the menopause, the question of high blood pressure comes up. If this were a common phenomenon, a relationship would be suspected; but in my own experience high blood pressure at the menopause is due to some special cause not related to the latter. Hence, if I find

the blood pressure too high, I set about to find the leading causal factor, and if such cannot be found, we evidently have nothing more than a case of so-called essential high blood pressure in which no causal factor of any kind can be isolated.

To those who cannot visualize that dysfunction of the menopause is able to affect the digestive system through the vagus, it is well to note that paroxysms of bronchial asthma may result in this manner.

Leaving the subject of the menopause and reflex irritation, attention must be directed to the possibility of mechanical compression of the lower bowel, especially in the case of a uterus enlarged, for example, by fibroids, or of adhesions between the left adnexa and pelvis, which are known to cause partial occlusion of the sigmoid. In compression by a fibroid uterus an additional factor may develop in an adhesive peritonitis. Even a simple retroflexed uterus bound down by adhesions may give rise to much rectal disturbance. At the present time a routine proctoscopic examination of all gynecologic patients ought to be urged.

I have already mentioned pelvic adhesions under adnexal disease and the subject comes up again under parametritis. There are two end-results: viz., an unabsorbed fibrinous exudate and the contracting form which is due to absorption and fibrinous contraction in the broad ligament. Either the paravesical, parauterine, or pararectal tissue may contract or the process may involve all jointly in a stellate formation. If an exudate forms at the lateral margin of the uterus, whether of the lymphatic or thrombophlebitic type, it may encroach on the sigmoid and displace the lower end of the bowel laterally; and if contracture occurs, there may result a partial or complete occlusion, either in the sigmoid or rectum. After absorption has occurred, the constriction may be released for the time being, although permanent narrowing may be the end-result. Bacterial penetration from the bowel may cause suppuration of the exudate or pelvic abscess which may burst into the sigmoid or rectum, leaving fistulas.

Primary parametritis may result from simple infection, trauma, or puerperal infection, the first two from the use of instruments, and especially from the traumatic effect of the curette. Enterogenous cases have already been mentioned, and the intestinal obstruction which may develop in this type may call for a colostomy. On the right side the pathology naturally differs much from that on the left, as in place of sigmoid and rectum there are the cecum and appendix as well as the terminal ileum to be considered. In cases of salpingitis and perisalpingitis as well as in cases of cystic ovary all of these structures may be involved jointly in adhesions, with obstruction and toxæmia. In such cases, originating in the ovary, the only symptom perhaps is pain, chiefly in the intestine from obstructive colic. Naturally any of the pathology mentioned above may occur after operations.

Insufficient attention is paid to the ileum, cecum, and sigmoid in surgery below the umbilical line. General neglect of the peritoneal toilet and careless pulling out of the walling-off pads are to blame for some of these complications which involve the genitals with the alimentary canal. In my experience a careless appendectomy may light up an ovarian cyst with unusual complications in women who have never presented any evidence of genital pathology.

On the left side we have the condition known as perisigmoiditis, which, while much less frequent than appendicitis, gives rise to a similar clinical picture and in the female may be complicated by adnexal disease. Perisigmoiditis as is well known accompanies diverticulitis, and the chronic form of the latter closely simulates cancer of the sigmoid. Diverticulitis, in setting up perisigmoiditis, naturally causes adhesive complications. The peculiar shape of the sigmoid and its proneness to lengthening and dilatation give large opportunities for adhesion formation and incidentally for kinking, partial obstruction, further dilatation, and more adhesion. It must be borne in mind that inflammation is not absolutely necessary for adhesion formation which may result simply from the friction of newly apposed segments of bowel. In addition to adnexal disease adhesions may form in connection with a parametritic exudate. Another property of the sigmoid when not fixed by adhesions and when abnormally long and mobile is the ability to migrate to almost any abdominopelvic location and form adhesions of the most bizarre character. Naturally adhesion formation arrests the tendency to wander farther. I have found it adherent in the right iliac fossa. In some cases, of course, the sigmoid is pushed out of place by large tumors.

Attention should be called to the close relationship often found between appendicitis and menorrhagia, so that when the latter is present without apparent cause, we should investigate the possibility of latent appendicitis. Appendectomy has sometimes been followed by the disappearance of menorrhagia and even of dysmenorrhea. In such cases the pathology involved probably has to do with passive congestion of the pampiniform plexus or some adnexal complication in which adhesions have interfered with the circulation.

I have already expressed the belief that a proctosigmoidoscopic examination should always be made by the gynecologist as a routine measure. Should sigmoiditis be found, it will very probably involve the pelvic viscera secondarily. Conversely, in adnexal disease the escape of saprophytes or septic germs through the fimbriated extremity may set up pelvic peritonitis, with adhesion formation between the posterior wall of the uterus and anterior wall of the rectum. In such a case we may encounter rectal tenesmus, mucoid discharge from the rectum, pain, and on examination, much tenderness. These acute symptoms may later be replaced by the effects of contraction of the

adhesions which cause retrocession or retroflexion of the uterus, the displaced fundus uteri being forced against the rectum.

The general syndrome of utero-enteric pathology comprises back-ache, menorrhagia, marked constipation, meteorism, etc., and this primary symptom group may be followed by a great variety of secondary pathology comprised under intestinal toxicosis, neurasthenia, and many forms of organic disease of the alimentary canal.

I have alluded only casually to the secondary effects of large tumor masses and cysts originating in the female genitals upon the functions and structure of the alimentary canal. It must be pointed out, however, that unless the pressure is exerted within the true pelvis (upon the sigmoid and rectum), the digestive tract is not much menaced. This we can understand in connection with the pregnant uterus, which does comparatively little damage to the parts of the alimentary canal above this level and even does not greatly disturb the functions of the latter during gestation. In the same manner an enormous simple myoma or ovarian cyst may exist without causing the slightest disturbance of the digestive tract.

Owing to the thinness of the rectovaginal septum, cancer of the cervix, which implicates the latter, soon leads to fistula formation, and the natural extension along the parametria may also extend to the rectum. Cancer of the vagina rapidly extends to the rectum with fistula formation. The converse, however, is not true, for cancer which is primary in the rectum involves the genitals only very late in the disease. Ovarian cancer, which is usually metastatic, involves the intestine in adhesions. Not often encountered by the operating surgeon but familiar to the pathologist is the mass of adhesions and distortions seen in the last stages of intestino-peritoneal tuberculosis and secondary carcinosis of the peritoneum. These may involve alike the intestinal and generative organs, especially the former, causing multiple strictures of the small bowel. Owing to the moribund condition of the patients, such conditions naturally do not present much clinical interest.

When considering the reciprocal relations between the reproductive and alimentary systems, it should always be borne in mind that either one may be involved primarily, the other participating as a secondary manifestation. It is equally true, however, that the involvement of both systems may be a pure coincidence, although with the intimate relationship an affection of one system may make itself felt on the other. Naturally certain predisposing factors may encourage the development of disease of both systems at the same time, including anemia, general ptosis, and the habitus asthenicus. The physical type and race may also constitute a factor. Thus in the asthenic, more or less infantile type, we may see certain gastric disorders before puberty and when the latter develops there may be an association of symptoms involving both systems—on the part of the reproductive

system, menstrual anomalies; on the part of the digestive system, anorexia, nausea, and vomiting. An objective examination may show in the reproductive system stenosis of the cervix, hypoplastic ovaries, and other evidences of infantilism, while the use of the sigmoidoscope may reveal the presence of colitis. In addition the nervous system, including the autonomous portion, and the endocrine system may participate and cause all sorts of nervous and systemic manifestations, such as migraine and hysteroid symptoms. Finally it may be shown, in general, that menorrhagia diminishes gastric secretion even to anachlorhydria, while the opposite state may cause hyperchlorhydria; although if menstruation is within normal limits, no effects are produced in the alimentary system. Vicarious menstruation may be expressed as hematemesis, bleeding from the lips, etc., which have been known to persist beyond the menopause.

At the menopause there is a marked tendency for the development of nervous symptoms referred to the stomach and associated with the vagus tract. Painful and paresthetic sensations may be felt as high as the tongue, and marked hyperacidity is present as a rule. These sensations may simulate those due to gastric ulcer and, according to some authors, the latter is actually present in one group of cases. It is hardly necessary to point out the gastric symptoms of gestation, since these are so well known. There are several motivations—reflex, autotoxic, psychogenic—so that it is difficult to isolate the component which corresponds to the gastric disturbances of puberty and the menopause; nor can we explain why the primipara is so much more apt to suffer from gastric symptoms than the multipara. The fact that occasionally a pathologic nongravid uterus can mimic the nervous symptoms of pregnancy has always been accepted as evidence that a reflex factor is involved, although the mere presence of the ovum in the uterus can hardly be the eliciting factor, since the reflex symptoms are present in the same degree in ectopic gestation. The rôle of the puerperium and of lactation in causing disturbance in the functions of the alimentary canal is causal and indirect.

Gynecologic ailments were said by some of the older clinicians to cause "uterine dyspepsia," but at the present time this relationship is regarded as problematical, and the nervous manifestations may be traced to other sources. Formerly there was not the tendency or the knowledge available to exclude various factors, such as endocrinic on the one hand or an erroneous sexual life on the other (coitus interruptus). Moreover, there may have been organic disease of the stomach in some of these cases.

Let us take at random an example of genital disease as a cause of gastroenteric disease. A woman has genital prolapse and subinvolution of the uterus, with retrodisplacement and fixation in this position by adhesions. When she lies down at night, she may suffer sooner or later from severe backache, abdominal pain, and vomiting. If she

sits up in bed or gets up, the disagreeable symptoms gradually wear away. The latter, by the way, frequently rouse the patient from her sleep. The motivation in this kind of case is reflex peritoneal irritation from the fixed adherent uterus. Uterine prolapse may also disturb the gastroenteric tract in a reflex manner.

Conversely let us take an example of gastroenteric pathology causing genital disease. Here it is usually some portion of the lower half of the alimentary tube which is at fault. Of functional anomalies obstipation may be cited, for efforts at defecation tend to cause or increase prolapse of the uterus, and under organic lesions appendicitis and its adhesions may be responsible for right adnexal pathology.

In certain cases as already mentioned both systems may be affected synchronously from the same causal factors. Here belongs especially visceroptosis which may affect the viscera of both systems. A psychogenic substratum may also make itself felt and so in general may any general cause of diseased conditions whether anemia, infection, or toxemia.

In general diagnosis, therefore, we have to isolate all possible general causes of disease to determine the rôle played in causing pathology of either system; and at the same time we must show how one system can cause or aggravate the disease in the other through its own abnormalities.

139 WEST SEVENTY-EIGHTH STREET.

CASE OF INTESTINAL OBSTRUCTION SIMULATING TWISTED OVARIAN CYST

BY ABRAHAM J. FLEISCHER, M.D., NEW YORK

THIS case is presented in the hope that a clinical experience, which fortunately had a happy culmination, might prove profitable to others encountering the same condition.

Mrs. B. C., thirty-two years of age. Previous history: She was frequently constipated, requiring the use of laxatives; she complained of frequency of urination. Menstruation began at the age of twelve, twenty-four days type, flow lasting three to four days, moderate in amount. Her last regular period began on September 16, 1927. Dysmenorrhea, menorrhagia, or metrorrhagia were never experienced. First pregnancy, delivery and puerperium were uneventful. One induced abortion in 1919, shortly following the birth of her baby. Recovery was uneventful. Her gynecologic history revealed a state of sterility since the time of her abortion. There were no previous illnesses or operations. The family history revealed the death of one brother due to intestinal obstruction.

On October 3, 1927, I was called to see this patient, at three o'clock in the afternoon. When I arrived, I was compelled to wait some ten minutes before I could see the patient, who had gone to the lavatory. I mention this fact, because of the striking disproportion between the clinical picture and the operative findings. She gave a history of having had an acute attack of pain in the left lower quadrant of the abdomen at 9 o'clock that morning. This was followed by

fainting. There was no nausea or vomiting. She had just had a normal bowel movement, which she said was not blood-stained.

Physical examination revealed an adult female, apparently not acutely ill. Rectal temperature 99°, pulse 80, blood pressure, 120/80. Examination of the head, neck, and chest showed no abnormal findings. The abdominal wall was markedly obese and decidedly tender over the left lower quadrant. Corresponding to this area of tenderness, a large mass, about six inches in diameter, was definitely outlined. It was movable, and imparted a cystic feel. Vaginal examination did not establish any connection of this mass to the uterus, which was small, firm, and freely movable. No adnexal pathology could be elicited, other than that of the abdominal findings.

With the history of acute onset of pain, accompanied by fainting and the physical findings, a diagnosis of twisted ovarian cyst was made, and the patient prevailed upon to go to the hospital for immediate operation.

At 6:30 P.M. of the same day, laparotomy was performed under ether anesthesia. On first examination of the abdomen and pelvis, through a midline incision, no apparent pathology could be detected. The uterus and ovaries were brought into the field of operation, and were found to be normal. Upon further inspection, through the aid of bimanual palpation, one hand within the abdominal cavity, and the other over the abdominal wall, the mass was found to be attached to the anterior abdominal wall by a thick band of connective tissue. By means of finger dissection, this mass was separated and brought into the line of incision. The dissection was not difficult, excepting at the point of attachment of the tumor mass to the abdominal wall, where this firm band was encountered. The mass consisted of about eight inches of black intestine, involving the lower portion of the ileum, about which, lying in juxtaposition, was healthy jejunum and ileum. The apparently gangrenous intestine was devoid of visceral peritoneum at a point, midway, corresponding to the area of attachment of the band. The intestinal wall presented numerous hemorrhagic areas, varying from $\frac{1}{4}$ to $\frac{1}{2}$ cm. in diameter. The distal mesenteric vessels, at the line of attachment of mesentery to ileum, were thrombosed at four different points. These thrombi ranged from $\frac{1}{2}$ to 1 cm. in diameter. With the aid of hot packs, the tone and luster of the injured gut returned, and so, fortunately, resection was not necessary. The intestine was repositioned, and the abdomen closed without drainage, after the appendix had been removed. During the first four days she had a temperature of 100.8°, after which her convalescence was uneventful. She was discharged after a two weeks' stay in the hospital with a postoperative diagnosis of an acute partial intestinal obstruction, due to an adhesive band, with secondary thrombosis of the smaller distal mesenteric vessels.

Five months after operation, the patient is well, and about her usual vocation, complaining only of occasional constipation.

One's curiosity, in a case of this kind, is naturally aroused by the peculiar pathology, and the more obscure etiology. The clinical findings of an abdominal mass are readily explained. A piling-up of healthy intestine about a diseased portion of bowel is only nature's expression of an attempt at a protective mechanism. Such a mass can very easily impart to the examining fingers the impression of an ovarian cyst. And when the obesity of the abdominal wall is so marked that a mass cannot be definitely determined one must rely on an area of dullness elicited by percussion. In April of 1927 I was called to see a case that presented the very same clinical picture as the one herein described. An unusually obese abdomen allowed of no

definite palpation of a mass, but percussion did reveal a definite area of dullness, upon which finding, together with the history, a diagnosis of twisted ovarian cyst was made and confirmed at operation.

The pathology in this case is not a very unusual one. The kinking of the intestine at the point of attachment to the abdominal wall, of necessity, impaired the circulation, with the resulting debility of the intestinal wall, bordering on absolute gangrene, expressed in the hemorrhagic appearance, discoloration and loss of luster. The thrombosis of the mesenteric vessels, to my mind, was strictly a secondary process to venous stasis, and is more elaborately elucidated by Aschoff's treatise on the causation of thrombosis in the blood vascular system.

What caused this band of adhesion extending from the intestinal wall to the parietal peritoneum? To explain this is not an easy matter. There was absolutely no evidence of an inflammatory or traumatic process in the uterus or its appendages. Can one dare to imagine, that, when this illegal abortion, referred to in her past history, was performed, the uterus was perforated, and the intestine injured at this point; and through the grace of God, the patient made an uneventful recovery, in spite of this abuse? Also, through nature's miraculous powers, healing of this injury was so complete, that it even defied the minutest gross examination of the pelvic organs. Such occurrences have been known in the past. Or shall we look for an explanation to Pfahler's statement: "Localized peritonitis resulting in adhesions is a common condition and while it must often be present without producing any symptoms it is a pathologic condition that should be considered in all obscure abdominal cases." Still another possibility is a primary intestinal phlegmon, akin to that described by Metge. A more abstract explanation would be to resort to Lave's theory: "These bands about the ileum cecum, etc., are embryonal remains . . . persisting folds in the evolution from so-called 'adhesions' in embryo . . . which under normal conditions would disappear."

CONCLUSIONS

A moribund condition of the patient is not an essential requirement in arriving at a diagnosis of intestinal obstruction.

2. It is not an uncommon occurrence for intestinal obstruction to simulate a twisted ovarian cyst, or any other pelvic condition.

3. The pathology resulting from intestinal obstruction may be entirely out of proportion to the clinical picture, in the early stages.

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A FOUR-BLADED SPECULUM

By H. M. NELSON, M.D., DETROIT, MICH.

(*Department of Gynecology and Obstetrics, Henry Ford Hospital*)

WE DEvised this four-bladed speculum in order to get a better exposure of the cervix for local treatment, especially cauterization. The chief difficulties in office cauterization are faulty exposure of the cervix and imperfect protection of the vaginal walls during the treatment. The ordinary bivalve speculum permits the lat-

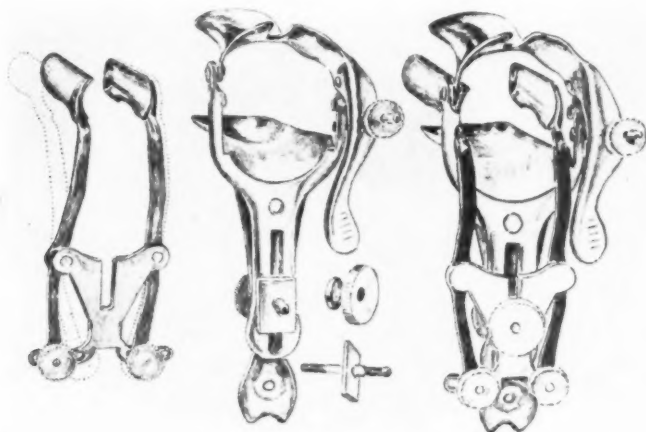


Fig. 1.—Anteroposterior view, showing set screw and adjustability of lateral speculum.

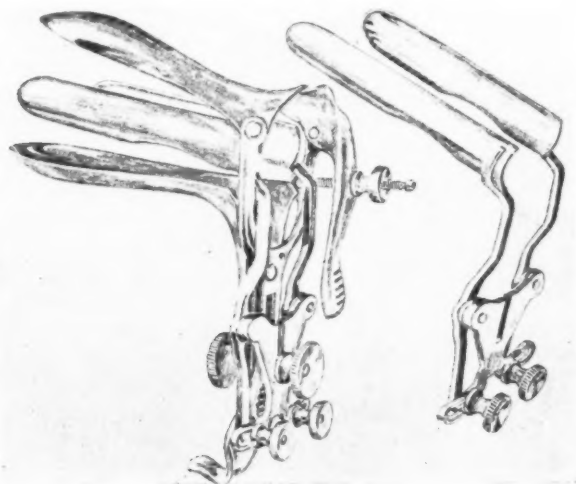


Fig. 2.—Lateral view.

eral vaginal walls to roll in, obscuring the view and causing severe pain from close proximity of the cautery to the vaginal wall. The tubular speculum is not adjustable and is often too small to give proper exposure.

Our instrument consists of an ordinary bivalve speculum with a special set screw attached, so that a lateral bivalve speculum can be inserted. Either blade of the lateral retractor is adjustable and it can be opened even wider than the Graves speculum, thus holding the edges of the vagina apart, giving an excellent view of the cervix.

We have made separate instruments for the medium and large bivalve specula. For general work the medium speculum is the more useful.

The illustrations give both lateral and anterior views.

The latter shows the set screws to which the lateral speculum is attached. It also illustrates the slot and the two set screws on the attachment which permit lateral and anteroposterior adjustments.

We wish to acknowledge the help of Mr. Alfred H. Schmidt, instrument maker for the hospital, who made the speculum and offered very many valuable suggestions.

THE FLUCTUATION OF BLOOD SUGAR BEFORE AND AFTER AN ECLAMPTIC CONVULSION

By JOHN M. LAFERTY, M.D., J. A. NARK, M.D., AND J. J. SWEENEY, M.D.

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(From the Obstetric Department, St. Mary's Hospital)

DR. PAUL TITUS, of Pittsburgh, has demonstrated that a hypoglycemia, relative or absolute, precedes an eclamptic convulsion. The object of publishing these observations made on one patient is to add to his series. A brief history of this case is as follows:

The emergency patient was a twenty-eight-year-old para v admitted 4/15/28 in eclampsia starting after the end of labor. Her first pregnancy and labor were normal, but were followed by two miscarriages and one premature labor. Previous medical history was poor, for among other diseases she had had diphtheria, scarlet fever, an appendectomy, and mastoiditis. She menstruated at intervals of from sixty to ninety days, the last occurring 8/2/27. Her prenatal course was not supervised and discloses: headache, edema, vertigo, lack of exercise, and a probable gain of 48 pounds in weight. Twenty-four hours before labor there was a period of visual disturbance. Her labor at home was said to be spontaneous, child living. The first convulsion occurred forty-five minutes after the end of her labor and was followed by headache and vomiting but no coma. The second convulsion occurred ten hours after the first; the third after an interval of eight hours and resulted in coma; the fourth occurred shortly after admission and three and a half hours after the preceding convulsion. She had two more convulsions, as listed in

the table. The patient recovered. Treatment: conservative (Rotunda method) plus glucose infusion (Titus).

Physical examination on admission: Coma, followed by convulsions as listed, tongue bitten, myocarditis suspected, pulmonary edema slight, thyroid small, liver not palpable, varicose veins, Babinski sign positive. Urine contained many hyaline and granular casts, marked trace of albumin, a large increase in urobilin and urobilinogen, and an initial output of 500 c.c. Other physiologic data are given in the accompanying table.

TABLE SHOWING VARIATION OF BLOOD SUGAR

DATE	HOOR	STATUS	BLOOD SUGAR	GM. GLUCOSE GIVEN	GLYCO-SURIA	BLOOD CREAT.	BLOOD UREA
4/15	12:30 P.M.	Coma	42	before	—	7.0	20
	3:30 P.M.	"		25			
	3:45 P.M.	Convulsion, 3 m.		25			
	4:15 P.M.	Convulsion					
	4:45 P.M.	Coma	38				
	4:57 P.M.	"	42				
	5:14 P.M.	"	36				
	5:15 P.M.	Convulsion					
	5:16 P.M.	Convulsion ending	42				
	5:22 P.M.	Coma	39	25			
	6:30 P.M.	"		25			
	8:30 P.M.	"		25			
	11:00 P.M.	"		50			
4/16	11:30 A.M.	Semicoma	220		+	1.9	18
	5:00 P.M.	"	320				
4/18	2:00 P.M.	Rational	39		—		
4/19	1:00 A.M.	Restless and drop in blood sugar of 4/18		50	—		
	11:00 A.M.	Rational	90	i.e., 10 hr. after reception of 50 gm. glucose			
4/20	11:00 A.M.		110				
4/25	11:00 A.M.		97				

1332 SPRUCE STREET.

REPAIR OF VESICOVAGINAL FISTULA

By ARTHUR E. HERTZLER, M.D., HALSTEAD, KANSAS

THE following plan of procedure for the repair of vesicovaginal fistula has served me without fail for more than twenty years. The essential feature is that a fold of vaginal mucosa is so prepared that a broad surface is brought in coaptation which is protected from contamination through the bladder by means of staple sutures.

The first steps in the operation do not differ from the more or less classical procedures. The vaginal wall about the fistula is elevated (*a*, Fig. 1) so that the freshened surfaces may be brought into contact and inverted into the bladder by a row of No. 00 chromic catgut sutures (*b*, Fig. 1). This row is inverted still further by a second row of similar sutures, either continuous or interrupted (*c*, Fig. 1; also compare *d*, Fig. 2).

The mucosa of the vagina is now elevated from the bladder (*d*, Fig. 1). This separation should be made to extend for a centimeter or two, depending on the size of the opening to be closed. These flaps must be mobilized so that they can be brought together without tension.

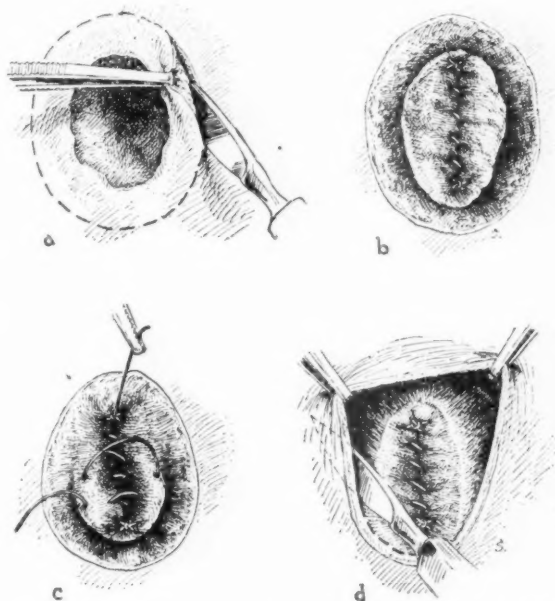


Fig. 1.—Preparation and inversion of the bladder cuff: *a*, Incision about the fistula forming a tube of tissue; *b*, first line of sutures inverting the cuff; *c*, second line of sutures burying the first line; *d*, elevation of the vaginal from the bladder wall.

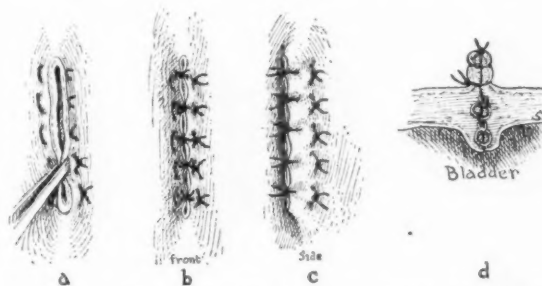


Fig. 2.—Approximation of the vaginal flaps: *a*, Staple sutures are placed at the base of the flaps about 1 cm. or more from the edge; *b*, the edges of the flap are brought together by delicate interrupted sutures; *c*, the operation is finished showing both lines of sutures properly placed; *d*, cross-section of the finished operation showing both lines of inverting sutures, the staple sutures above and the approximating sutures closing the vaginal flaps.

The bases of these flaps are brought together by staple sutures of silkworm-gut (*a*, and *c*, Fig. 2). They must be placed at least a centimeter from the edge and brought snugly together. The line of sutures must not be so tightly drawn together as to disturb the circulation. The edges are now brought together with silkworm-gut

sutures (*b* and *c*, Fig. 2). This line must be delicately placed so as to leave sufficient tissue between this and the preceding row of sutures, for it is on the vascular integrity of this tissue that the success of the operation depends.

A cross-section of the line of repair (*d*, Fig. 2) shows the first two lines of sutures inverting the bladder wall into the bladder, while the staple suture inverts the vaginal wall into the lumen of the vagina. The coaptation sutures uniting the edges of the bladder wall show a too generous bite in the figure. These should include as little tissue as possible.

A permanent catheter is placed and is allowed to remain a week or ten days. Care must be taken lest the lumen of the catheter becomes occluded.

The staple sutures remain in position about three weeks.

BILATERAL TUBAL PREGNANCY WITH RUPTURE OF BOTH TUBES

BY HAROLD H. JOHNSON, M.D., AND JOSEPH S. DIASIO, M.D.
NEW YORK CITY

(From the Gynecological Service of Dr. P. H. Williams, Lincoln Hospital)

A REVIEW of the literature for the past seven years revealed reports of ten cases of bilateral tubal pregnancy. In one of these cases rupture occurred in both tubes. Therefore, we believe, the condition is rare enough to justify the report of the following case.

Mrs. C. C., aged thirty-seven, married ten years. One miscarriage nine years ago and one forceps extraction two-and-one-half years ago. Menses regular for the past year. No operations.

The patient was admitted to Lincoln Hospital on February 16, 1928, complaining of occasional attacks of cramp-like pain in the lower abdomen, especially in the left lower quadrant, for the past six weeks. Three days before admission she was seized with a very sharp pain in the left lower quadrant with a simultaneous sensation of faintness, and has had several severe attacks since. Vaginal bleeding, spotty in nature, but never very profuse, has persisted since onset. She had her last regular menstruation on November 21, 1927, and flowed twelve hours on December 19, 1927. Several days after the onset of the present illness, the husband called his private physician who treated the patient for miscarriage, later for "incomplete abortion," up to the day of admission to the hospital.

The patient was pale with a lemon-colored look. She appeared to be in a state of collapse. There was a severe anemia of the mucous membranes and conjunctiva. The head and neck were normal and the nose and throat clear. The heart was normal in size and position, the rate rapid, the rhythm normal, but no murmurs were heard. The lungs were negative except for a few mucous râles heard over the larger bronchi. The abdomen showed a fullness in the lower part, tenderness on pressure in both lower quadrants, and general pseudorigidity. Vaginal examination disclosed a soft, tender uterus, a boggy, cystic mass filling the pelvis, exquisite

tenderness in both fornices, and a slippery, dark, bloody discharge from the cervix. The temperature was 98.2° F.; pulse 96. The patient looked ill.

Urinalysis of a voided specimen disclosed: specific gravity 1030, reaction acid, albumin trace, sugar and casts negative, pus cells two per high power field, a few calcium oxalate crystals, and a few epithelial cells. The blood examination showed: red cells 2,560,000, hemoglobin (Dare) 40 per cent, leucocytes 13,100, polymorphonuclears 74 per cent, large lymphocytes 1 per cent, small lymphocytes 25 per cent.

A clinical diagnosis of ruptured ectopic gestation was made and the patient ordered to the operating room.

The abdomen was opened under ether anesthesia. The left tube was found attached to the fundus uteri by fresh adhesions. The distal half of the tube was distended, with an opening 3 cm. long, filled with blood clot and organizing material, and covered with omentum and small intestine. The right tube was enlarged and, with the ovary, was adherent to the uterus, bladder and small intestine. Both tubes were removed and a ventral suspension performed.

Examination of the specimen showed, in the left tube, a distention of the distal half, with an obvious tear, filled with blood clot. The right tube was distended throughout. In the middle third was a tear $\frac{3}{4}$ cm. long with a blood clot protruding through it. Section showed chorionic villi and hemorrhage.

The patient made an uneventful recovery and left the hospital February 29, 1928 (thirteen days after the operation) having been up and around the ward for two days, feeling fine and happy.

119 EAST EIGHTY-FOURTH STREET.

EARLY ADENOCARCINOMA OF UTERINE BODY COMPLETELY REMOVED BY CURETTAGE

By SAUL SEIDES, M.D., F.A.C.S., BROOKLYN, N. Y.

IN AN article entitled "A Plea for Early Diagnostic Curettage and Routine Microscopy of Curettings for the Detection of Adenocarcinoma of the Uterus," appearing in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, February, 1928, Dr. L. J. Ladin reports two cases, in addition to the three previously reported by him, of adenocarcinoma of the uterus, limited to the endometrium. In four of these cases the curette succeeded in completely removing the malignant growth.

In reviewing the literature Dr. Ladin brings out the following facts:

In 1915 no record of a similar case could be found in American or British literature, while 19 cases were previously reported in German and Austrian literature. Shortly after the publication of his paper, in 1915, similar case reports began to appear. In France, Muret reported four cases in 1915. In Holland, Van de Poll reported one case in 1917. In this country, R. T. Frank reported a case in 1915, S. Wiener, one case in 1917, and Palmer Findley two cases in 1917. Since then a search of the literature fails to show the record of a case.

The case reported here makes the number of cases on record in American literature 10, and the total number reported, 34.

Mrs. T. J., aged forty-one, was admitted December 5, 1927, to the United Israel-Zion Hospital, complaining of irregular bleeding of seven months' duration. The patient had been married nineteen years, para vi, gravida vii, last pregnancy six years ago. Family history negative. For the last five years the patient has been under treatment for diabetes. Operated on twice for glaucoma seven years and two years ago. Menses regular, every four weeks, lasting five days, flow moderate, no intermenstrual discharge. For the last seven months her menses changed, the flow appearing more frequently and at irregular periods. Last menstruation occurred November 19, 1927, and lasted five days. November 30 the bleeding re-appeared and has continued since.

Physical examination, negative.

Vaginal examination: perineum slightly lacerated, pelvic floor fairly firm. Vagina filled with clots. Cervix markedly lacerated. Uterus enlarged to the size of a six to eight weeks' pregnancy, retroverted. Adnexa not palpable. R.B.C., 4,000,000;

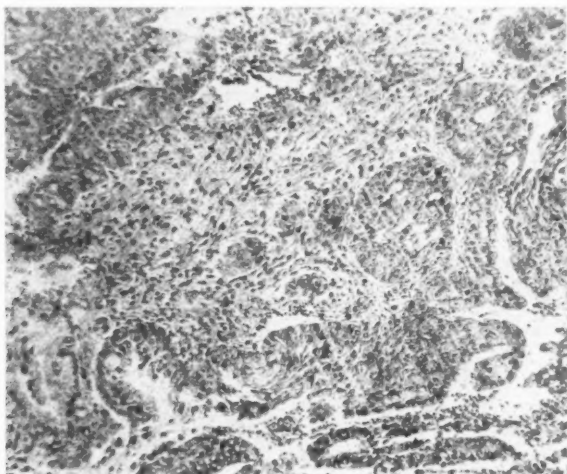


Fig. 1.—Photomicrograph showing solid groups of squamous cells partly infiltrating the stroma. There is a direct connection between the cylindrical epithelium of the uterine glands and the squamous epithelium.

Hb., 78 per cent; W.B.C., 9,000; polys, 74 per cent; urine, 1.4 per cent sugar, otherwise negative. December 6, I performed a diagnostic curettage, and the specimen was submitted for microscopic study to Dr. M. A. Goldzieher, who on December 9 reported as follows:

Sections from the curettings showed a markedly hyperplastic uterine mucosa. The interstitium of the mucosa is cellular. There are quite a few lymphocytes, plasma cells, and polynuclear leucocytes. The uterine glands are numerous. Their longitudinal sections are tortuous, whereas the cross-sections are often dilated. Many of these tubules are lined with epithelium in several layers, showing evidence of hyperplastic proliferation. Yet the irregularities of the individual cells and particularly of their nuclei are not very pronounced. In between these hyperplastic tubules quite a few scattered areas of squamous cell epithelium can be met with. These groups of epithelial cells are within the stroma of the uterine mucosa. Occasionally they are in connection with uterine glands, the epithelium

of which shows gradual metaplastic transformation. The individual cells of the fully differentiated squamous cells are much more irregular than those of the uterine glands.

Diagnosis: Early adenocarcinoma of the uterine mucosa.

On the strength of this report I performed panhysterectomy under spinal anesthesia and submitted the specimen to Dr. Goldzieher whose report follows:

Examination of the uterus after its surgical removal showed a fairly well regenerated mucosa on its inner surface. There are only a few areas on which the regeneration of the mucosa still lags behind. The stroma of the new mucosa is

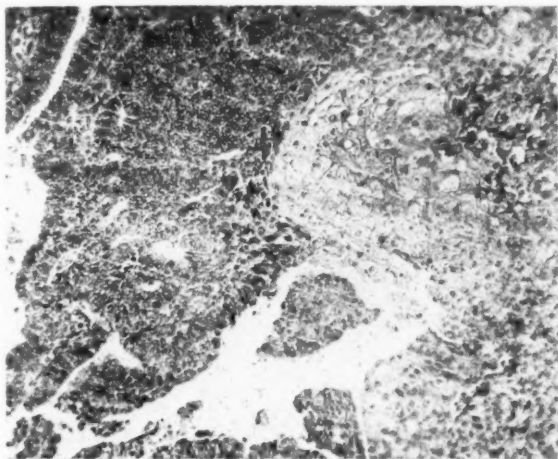


FIG. 2.—Photomicrograph showing solid nest of keratinized squamous epithelium adjacent to intensely proliferating tubular glands. The epithelium of the tubular glands is anaplastic.

diffusely infiltrated with round cells. The uterine glands are numerous, slightly tortuous. Their epithelium does not reveal any particular irregularities. There are no epithelial elements to be found in the musculature of the uterine wall. Sections taken from the various parts of the uterine wall showed quite analogous behavior.

Diagnosis: Hyperplastic endometritis; no carcinomatous tissue left.

The patient's convalescence was uneventful, and she was discharged from the hospital on the fourteenth day after operation, in good condition.

4510 TWELFTH AVENUE.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 8, 1928

DR. PERCY H. WILLIAMS reported a case of **Endometriosis in an Abdominal Scar Following Cesarean Section.** (For original article see page 102.)

DISCUSSION

DR. B. P. WATSON said that Bonney and Davidson reported a case recently where this condition followed in the abdominal scar after an operation for myomectomy.

DR. I. C. RUBIN instanced a case of what one might call a miniature cesarean section, an abdominal anterior hysterectomy, in a patient where not only was the uterus emptied of a two months' pregnancy but also a ligation of the tubes for permanent sterilization was done. The uterus was sutured to the abdominal wall. She developed an endometrioma of the abdominal wall which gave her symptoms of pain and swelling on and off for four years. Dr. Rubin removed the lesion without entering the general peritoneal cavity and she has been free from her symptoms since then.

The mechanism by which the endometrial tissue is transplanted or dislocated into the abdominal wall, in addition to that mentioned by Dr. Williams, is possibly by another method. Dr. Rubin believed that where one fixes the uterus to the abdominal wall either after a myomectomy or after emptying a gravid sac, the suture line sometimes gives with or without a hematoma forming between it and the peritoneum. The endometrial particles can thus escape into the abdominal wound. This is more likely than that the suture drags the endometrium into the abdominal wound.

The point Dr. Williams brought out when he spoke of the possible way in which the serosa gives rise to endometrial cysts, has been definitely demonstrated by Schiller of Vienna, who calls attention to a pathologic process which he terms "prosoplasia," and conclusively shows that endothelium can undergo changes from the flat endothelial cell type to the low cuboidal and high cuboidal cell resembling the endometrial cell in every respect, including cilia. This process can affect the cells arising from the endothelial lining of the serosa, the peritoneal covering of the uterus, or from the endothelium of the lymphatics.

DR. W. H. CARY believed that there is another method by which implantation could happen easily in the fixation of the uterus. Most of us in bringing the uterus up into the abdominal wound for denudation and placing of sutures, use a sharp tenaculum forceps to take hold of the uterus, which very possibly pierces the body of the uterus and enters the mucosa, and that portion of the uterus is the one that is usually brought into coaptation with the muscle at the time the fixation is done.

DR. E. W. HOLLADAY stated that recently at Bellevue Hospital a case was observed in an unmarried girl, operated on in some other hospital two years before. Ever since then, every time she menstruated blood was discharged from the wound. They were unable to identify a true fistula there on subsequent operation. Dr. Holladay asked whether this was a similar case.

DR. WILLIAMS (closing) said in answer to Dr. Holladay that in the reports of these cases there were none described where there was an actual discharge of fluid from the tumor itself.

Answering Dr. Rubin, he stated that the serosa has been described as developing all sorts of epithelial tissue, but it would seem that this peculiar type of tumor, if it had to do with the endothelium, would be found in males as well as in females, and he did not know that one has ever been described in a male.

DR. J. C. LITZENBERG, of Minneapolis, Minn. (by invitation) presented a series of **Gross Microscopic Sections From Specimens of Ectopic Pregnancy.**

DR. J. L. HUNTINGTON, of Boston, Mass. (by invitation) presented a **Review of the Pathology in 104 Consecutive Miscarriages in Private Obstetric Practice.** (For original article see page 32.)

DISCUSSION

DR. GEORGE L. STREETER claimed that there are all kinds of eggs. He then showed a series of slides illustrating that throughout a great variety of plant and animal forms there has been demonstrated to exist a wide variation in the degree of vitality of seeds and eggs. Among the mammals that have plural births and particularly those with large litters, it has been proved that regularly from 20 to 30 per cent of the fertilized eggs fail to develop properly, and the blame can only rest on the male or female zygote. Dr. Streeter went on to say that in the human being we have to look at it in a rather particular way. In certain families there is a poor strain of eggs. We might expect certain patients habitually to ovulate eggs of poor vitality which develop only when other things are most favorable, or never at all. In other families some eggs are defective, so that they alternate between successful pregnancies and abortions. Some women seem to ovulate extraordinarily vital eggs and become pregnant at every opportunity; they are prolific and mothers of large families.

Men differ in constitutional vitality. Some men grow to old age, living a long, vigorous life. They abuse themselves; they overeat; they seem to work too hard; they do all the wrong things; maybe they take no exercise; yet they seem to live to be old, vigorous men. Those are good eggs. The average man reaches the age of fifty or sixty. Some live only until they are twenty and then fall by the way. Of course, others die in childhood, and there is a great mortality in the first year of life.

It seemed to Dr. Streeter that many of Dr. Huntington's cases are instances where the vitality is so poor they cannot get through the mechanism of development. To develop all the organs is a considerable task. Many of the eggs never accomplish that. There are more deaths in the first week of development of the ovum than at any other time and these deaths are never recognized, because there could have been no other evidences of pregnancy. It is in the very earliest specimens, if we could only get them, where we would find the greatest mortality.

DR. J. C. LITZENBERG said that in his clinic basal metabolism studies of several thousand women were made and among them several hundred women showed a moderately low basal metabolism. It seems reasonable to suppose that this would have an effect on conception and the ability to carry the product of conception, when we stop to think that in low basal metabolisms, like exophthalmic goiter, conception is rare, and conversely in myxedema we expect sterility. Therefore, we

might well conclude when a patient borders upon myxedema or on a high basal metabolism that we might get a relative sterility.

A study showed that in the women with a low basal metabolism the number of their children was much below those with normal basal metabolism. There were more living children per mother in those with normal basal metabolism, and among the women with low basal metabolism (minus 12 or 15, or 24 or 30) an astonishing history of abortions was given; they had many, many more abortions per mother than those with normal basal metabolism. Having obtained this lead they continued the investigation in a longer series, and it has come out the same way—those with normal basal metabolism have more living children per mother and those with low basal metabolism have more abortions per mother.

DR. ELIOT BISHOP was struck by the heresy that neither retroversion, nor intercourse, nor automobiles have much to do with miscarriages. He wanted to know how often the doctor has Wassermann reactions done on private patients with no apparent lesion. He remarked that nothing was said about the subject of the bacillus of Bang or the *Bacillus abortus* as a cause of miscarriage; this has been worked up by the veterinarians a good deal and DeForest carried over the study among human beings some years ago.

DR. G. L. MOENCH said that years ago it was always the woman who was blamed in cases of sterility or habitual abortion, and he wondered if we are not still tending somewhat in the same direction and not stressing sufficiently the rôle of germ plasm defects in the male. Dr. Streeter, as biologist, probably takes it for granted that we remember the fact that the spermatozoon as well as the ovum may be poor, but this truth is rather often slighted by medical men.

For a number of years Dr. Moench had been investigating especially the male side of sterility, and it is quite remarkable what a relation there seems to be between the micropathology and the biometrics of the semen, and the clinical fertility. Conklin, of Quebec, working with the rooster, showed that sexual overloading or deficient physical condition of the animal influenced the hatching of the eggs. The number of eggs fertilized remained about the same, but the death rate in ovo, especially the late death rate, was tremendously increased. W. L. Williams, working with cattle, showed that the number of services required per achieved calf was a direct indicator of the fertility of the bull, and the greater the number of services required, the greater invariably the abortion rate.

In human beings the importance of the male germ plasm defects is very impressive. Not long ago he examined the semen of a man whose wife had had a child only a few months before. According to our standards, however, the semen was very poor. On questioning the woman it was learned that shortly after she had conceived, her husband had fallen off a ladder, had been in the hospital for six months, and still was in very poor physical shape. In another instance the semen of a man, whose wife had had a number of children and then several abortions, was definitely poor. Here it was found that the husband frequently worked from six o'clock in the morning until twelve o'clock at night.

Not only the morphology of the semen, but also the biometrics of the sperm head are often found abnormal in cases of habitual abortion. Instead of the normal, or Gaussian curve, which Dr. Streeter showed, we get curves which are flattened, irregular, and skew toward one side or the other. In one case of sterility where otherwise we could not find anything the matter with the woman or the man, the skewness factor of the curve obtained from measuring the length of the sperm heads was over five times the probable error; and in biometrics any factor more than four times the probable error is considered significant.

Dr. Moench said that he was at present trying to learn something about the morphology of the spermatozoa by dissecting them with a Chambers' microdissection instrument. He found variations of elasticity in different sperm heads, and cited these rather randomly chosen findings with a view of proving that it is important to keep constantly in mind that in every case of disturbed fertility the man must be considered as big a potential factor as the woman. The ovum may be poor but the spermatozoon may also be defective.

DR. J. M. MABBOTT asked whether the period during which the dead fetus is carried before expulsion has been a matter of study. In that connection he wanted to describe a case of a woman who had had two healthy children and who then became pregnant and was told by her obstetrician that she was developing all right. About two or three weeks later she was told that the fetus had died, and then, unfortunately, she was told again, "No, you are progressing favorably." This woman had an abortion with a complete sac, which Dr. Mabbott saw, being the first doctor present in the emergency, a spontaneous delivery. This was ten and a half months after the probable date of conception, and the fetus was certainly no more than seven weeks old, so that it had been carried after its death for probably over eight and a half months; at any rate, it had been ten and a half months since the last menstruation.

DR. HUNTINGTON (closing) said that he had Wassermanns done only on patients where abortion occurred, to determine the etiologic factor. He knew nothing about the question of infectious abortions.

As to the legal question in the State of Massachusetts there is no law whatever in regard to abortions. Unless it is a criminal abortion, the attending physician is not required to pay the slightest attention to it as far as the law is concerned, and the products of conception may be thrown away, or studied, or ignored entirely.

Dr. Huntington wanted to emphasize again the fact that it was highly probable that the male was responsible for a great many of these cases of defective germ plasma.

In connection with the length of time that the products of conception have been retained: in a paper that he read five or six years ago he stated that in 38 cases, 1 was retained two weeks after development ceased, 1 two and one-half weeks after, 4 three weeks after, 1 four and one-half weeks after, 5 five weeks after, 2 seven weeks after, 2 seven and one-half weeks after, 3 eight weeks after, 1 eight and one-half weeks after, and 1 ten months after development had stopped.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF MARCH 2, 1928

DR. LEO S. SCHWARTZ read a paper on **The Treatment of Uterine Injuries**. (For original article see page 66.)

DISCUSSION

DR. H. B. MATTHEWS said that undoubtedly the quicker these patients are operated upon after the injury, the better the chance of saving them. If the patient is in shock, naturally you stop the bleeding and treat the shock, and then endeavor to find out the extent and location of the injury. Many of these lower uterine injuries, particularly if they are into and within the confines of the broad ligament, need nothing more than control of the hemorrhage by pack and need no further operative procedure at this time.

As to the other class of injuries in early pregnancy, namely, the perforations, Dr. Matthews claimed that the earliest possible diagnosis of the injury, with opening of the abdominal cavity, is demanded, and where the rent is of considerable size, complete hysterectomy should be done, perhaps with conservation of one or both ovaries.

Dr. Matthews did not agree with Dr. Schwartz that the conservative procedure is the better, but that treating these perforations of the uterus is comparable to treating gastric or duodenal ulcer.

DR. ELIOT BISHOP felt that certain of these injuries can be treated conservatively, such as a clean case of incomplete miscarriage where the end of the sound had gone through. If the uterus is perforated and intestine or omentum is brought down, that is another proposition; we can liken that to a perforated duodenal or gastric ulcer. Dr. Bishop did not believe that one can liken a clean uterine fundus to the perforation of a dirty bowel.

There is one other type of injury Dr. Schwartz did not mention, which apparently has not been noted in the literature at all. During the process of curettement, we may, without knowing it, perforate the cervix between the internal and the external os, into the broad ligament, with an extremely exasperating hemorrhage from the big veins.

DR. C. A. GORDON called attention, in regard to the question of the conservative treatment of rupture of the uterus, to some figures presented at the last meeting. After analyzing 1805 cases of cesarean section, there were 11 cases of rupture of the uterus with 3 deaths. Three occurred after one previous section, one after two previous sections, and one after three previous cesareans. Three followed forceps, two followed version, and in one the etiology was unknown. The point is this: four had hysterectomy, and in seven the wound was resutured. The seven in which the wound was resutured all got well. The three deaths occurred in those that had hysterectomy. One case that had hysterectomy got well. The seven cases resutured all got well.

DR. A. KOPLOWITZ said that one is not always sure of having perforated the uterus because a certain degree of relaxation of the uterus occurs and the sound goes up pretty high without damage. Where there is any doubt we should give such a patient the benefit and leave her alone unless something has been pulled down, such as a loop of gut.

DR. H. M. MILLS recalled a number of cases where an intern was trying to curet the uterus for retained secundines, perhaps at the third month of gestation, when suddenly the curet went in up to the handle, and the fact became apparent that there was a perforation of the uterus. Such patients should be left alone, and Dr. Mills claimed he never saw one of them die.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF APRIL 13, 1928

DR. A. S. MACGREGOR presented a preliminary report on **The Effects on Blood Pressure of Pituitrin and Oxytocin in the Puerperium.**

Textbooks have handed down many obstetric statements which are not confirmed by clinical observations. It has been taught for years that it is dangerous to use pituitrin to secure uterine contractions in cases of toxemia because of its tendency to elevate the blood pressure and thereby possibly precipitate convulsions.

This hesitancy to use pituitary extract in the presence of elevated blood pressure prompted this study of the effects of the drug on blood pressure. In addition, a

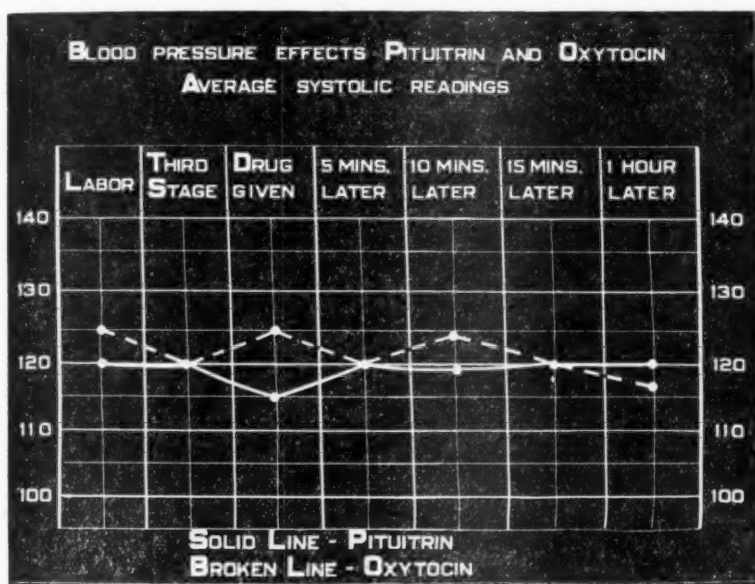


Fig. 1.

new preparation, oxytocin, has been used. This is said to be a pituitary extract free from the pressor element but still retaining the oxytocic principle.

From a study of the behavior of the blood pressure during the first, second and third stages of labor for several years, it was learned that in the course of normal labor, there are certain fairly constant variations. During the first stage, unless it is prolonged to the point of exhaustion, there was noted no change. In the expulsive stage, however, straining effort may raise the pressure five to ten millimeters only to have it fall again during the third stage.

In eclampsia, the fall following delivery is much more marked, a drop of 50 to 100 mm. often occurring with a subsequent slow rise to a mean safety level.

Does pituitrin alter this pressure reaction by suddenly raising the blood pressure or by maintaining it at a high level, thus defeating what appears to be nature's safeguard? This was the question in mind when undertaking this study.

This preliminary report is based on a study of sixty cases of which thirty received one ampule of pituitrin upon expulsion of the placenta and the remaining thirty, one ampule of oxytocin. These sixty cases all had blood pressures which were within the limits of normal during their pregnancies and labors, all received chloroform anesthesia and none of the deliveries were attended with any degree of shock sufficient to effect the blood-pressure readings. The pressure was noted during labor, during the third stage, immediately after the expulsion of the placenta (at which time the oxytocic agent was given) and at intervals of five, ten, fifteen, and sixty minutes thereafter.

The average blood loss in the cases in which pituitrin was given was approximately the same as that in which oxytocin was used and there seems to be very little if any difference in the rapidity of and duration of the action of these two drugs. Taking an average of the systolic blood-pressure readings as recorded, there was noted no marked nor uniform tendency for either of these drugs to elevate the blood pressure.

Only nine cases in which pituitrin was given showed a rise of 10 mm. or more. This rise occurred in five to ten minutes after administration of the drug, was not sustained and in no case was more than 16 mm.

Seven of the cases given oxytocin showed a similar elevation of 10 to 12 mm. and here again the rise was not sustained.

Both drugs were given to a number of toxic patients and there was no marked tendency to elevate the blood pressure nor to prevent the fall in pressure so often noted in such cases.

In several instances, more than one ampule of the drug was given. These cases also showed no marked tendency toward an elevation of pressure any more than did those in which only one ampule had been given.

DR. GEORGE GRAY WARD read by invitation a paper on **Radium Therapy of Carcinoma Uteri, Based on Ten Years of Clinical Experience and Results at the Woman's Hospital.** (See page 1 for original article.)

DISCUSSION

DR. WILLIAM SIDNEY SMITH said that the use of needles in conjunction with the tubes gave better results than tubes alone, screened in platinum. Dr. Ward screens his radium with brass, and probably gets some beta-ray action. Dr. Smith said that in the Brooklyn Hospital they screened radium with one millimeter of platinum, and did not get any beta-ray action. Possibly that makes some difference in the results.

Dr. Smith never considered it necessary to use a catheter in the bladder and his patients usually voided, even though they had a large pack in the vagina. The radium has always remained in place when it is used in the cervix with a small strip of narrow gauze about one-fourth inch wide packed around it, and the vagina packed full of gauze. At the Brooklyn Hospital it was not found necessary to sew the radium in the cervix, except for a metritis, and doing a repair of the cervix, or perineum at the same time. Dr. Smith then described the experiences with radium at the Brooklyn Hospital. There were only 68 cases of cervical carcinoma divided into the early and the advanced cases, numbering 56, and only 12 that could be considered early cases in which there was no demonstrable induration in the broad ligament, and in which the fundus was movable. In the 56 advanced cases they simply used radium as a palliative method of treatment. It stops hemorrhage, clears up a great deal of foul discharge, and above all, it makes the patient feel that something is being done.

Of these 12 early cases, one patient received radium and the disease spread very rapidly. This patient received a 2400-hour dose of radium. In one month the disease had spread like wildfire, and she died in six weeks, although Dr. Smith did not believe that the radium treatment had anything to do with her death.

G. I. Strachan, in the *Journal of Obstetrics and Gynecology of the British Empire*, for 1927, is sponsor for the statement that there is no evidence to show that radium treatment will make cancer spread.

In this group there were two cases of carcinoma of the cervix which were treated with radium, and later subjected to abdominal hysterectomy, both with unfavorable results. One of these patients had been operated upon, before she came under observation, for repair of the cervix and perineum. She apparently had no disease whatever. Three years later she came to the hospital with a history of slight spotting for six months, between periods. She was a widow, thirty-nine years old, and had not yet gone through the menopause. Carcinoma was suspected. There was absolute mobility of the entire uterus, with nothing to feel in the broad ligament. She was given a 2400-hour dose of radium. Spotting stopped, and one month later she was subjected to a total hysterectomy. There was no induration noted on operation. She made an easy convalescence. Three months later she came back to the hospital, and on routine examination a small nodule was felt in the scar. A small piece of it was taken off for biopsy, and immediately, she was given another 2400-hour dose of radium. She remained in good health for one year, when the disease began to spread out through the parametrium, and she died six months later.

Another case, a widow of thirty-two, came to the hospital with an extremely eroded cervix, and a large, hard fundus. She had bled considerably. We considered the diagnosis to be metritis rather than carcinoma. On investigation, however, it was found to be a carcinoma. She was transfused with 1000 c.c. of blood, and given a 2400-hour dose of radium. In one month the cervix had shrunk so much that it was normal in size. She was apparently perfectly well; she then had a total hysterectomy, and remained well one and one-half years when the disease spread out through the parametrium, and she eventually died.

At the Brooklyn Hospital the experience with radium, followed by total hysterectomy, has not been favorable. There were only two cases, but both terminated fatally.

The remaining 8 early cases were treated with radium in conjunction with the Byrne operation (long-continued roast with the cautery), and they form the best group of cases. Of these 8 patients, one died of recurrence two years after treatment (the only one). One has been lost to follow-up. One is in good health two years after treatment. One is in good health three years after treatment, one five years after treatment, two, seven years after treatment, and the other one is in good health eight years after treatment. So, according to the five-year rule, which Dr. Ward has laid down, there were 4 cases out of 8, or 50 per cent, alive and well, five to eight years after treatment.

Only two bladder fistulae were noted, and they occurred following the use of cautery. One was subsequently admitted to the Woman's Hospital and operated upon by Dr. Grad, who thought she was entirely free from cancer, and he cured the fistula by operation. The other patient still has the fistula. It is not a very bad one, and bothers her very little. She is one of the five-year cases, and is still in excellent health.

Comparing their statistics with those reported by Drs. John G. Clark, and Ferguson, in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*, February, 1927, who used radium similarly to Dr. Ward, in tubes and needles, screened in about the same way, they report that radium alone cured 4 out of 68 cases. Where

they amputated the diseased cervix with cautery and then used radium, they cured 6 out of 14 cases, or 42.9 per cent of five-year cures, as compared with 50 per cent at the Brooklyn Hospital.

In regard to the use of radium before operating in adenocarcinoma of the corpus uteri, they feel that if radium would slow up the cancer, these patients should be theoretically in better shape and better prepared to be operated upon a month later than if radium had not been used. Theoretically, it seems to Dr. Smith that it is a good thing to do.

There were 24 adenocarcinomas of the corpus, 11 fairly early cases, and 13 advanced, in which there was fixation of the fundus. Radium in the latter cases was used merely as a palliative measure. Radium alone was used on one early case with heart trouble, a poor operative risk. She remained in very good shape for four and one-half years, but then she had a recurrence. If the patient is in the operable class, Dr. Smith believes it is better to take the uterus out, and that the best time to do the operation is about a month after radium treatment. They had two deaths after hysterectomy, done after radiation, and operated early. Both patients died from sepsis and from general peritonitis.

Of the early cases of carcinoma of the corpus which were treated with radium and operated one month later, 2 have been lost to follow-up, 1 is in good health five and one-half years after operation, 1 four years after operation, 2 three years after operation, and 1 one and one-half years after operation.

Dr. Smith still uses 2400 milligram hours of radium within the corpus as a preliminary treatment to a total abdominal hysterectomy (one month later) in early cancer of the corpus uteri, because it seems wiser to curtail the cancer growth before subjecting the patient to a cutting operation. In this he differed from many authorities who believe the patient's best chance lies in an operation immediately after the diagnosis, or a presumptive diagnosis is made.

Notwithstanding what we have learned from Healy and others in regard to the way in which the different types of cancer cells react to treatment, Dr. Smith felt that the effect of radium on a particular case cannot be foretold. It may be brilliant or nil, so that prognosis should be guarded.

Where should cancer of the uterus be treated? Some say it should be treated only in large institutions where they have a large amount of radium. That may be true; perhaps they get better results in large institutions, but there are so few of them, and there are so many cases of cancer! Certainly the small institutions, or the institutions with only a small amount of radium, can do, as Dr. Ward has demonstrated, brilliant work with a moderate amount of radium used in repeated doses.

DR. C. A. GORDON asked Dr. Ward on what kind of a case and for what reason, since the radium results are so wonderful, he would do a Wertheim operation.

The five-year basis is an arbitrary method of tabulating cancer statistics. Dr. Gordon wondered whether anyone has followed the five-year cures and traced them for a longer period of time; whether, in short, that is a fair and safe basis for the determination of cure of cancer of the cervix or not. He also asked why in operations for cancer of the uterus we can sometimes save the most advanced cases and why it is not an uncommon thing at all to have a terrific spill of carcinoma tissue in the peritoneal cavity and still get a cure, and not have metastasis anywhere in the pelvis afterwards, if the patient should not be cured.

Moreover, is there any danger when passing a needle through the cervix of carrying through from the cervical canal any cancer cells to the blood vessels, and so carrying the carcinomatous process outside the cervix?

DR. WARD (in closing) wanted to congratulate Dr. Smith on getting 50 per cent of cures in his early cases. The trouble is we see so few early cases.

As to the use of the self-retaining catheter, Dr. Ward said that early in the work considerable trouble was caused by the fact that the nurse could not find the urethra to catheterize the patient, and the patient could not urinate with the vagina packed tightly with gauze. It is essential to keep the bladder or rectum as far as possible from the radium. The catheter works satisfactorily, and it never bothers the patient. Furthermore, where radium is used in the fundus of the uterus, it is well to keep the bladder collapsed and empty all the time, as the distended bladder would lie close to the radium in the fundus. The catheter in situ has been a very valuable aid in preventing vesical irritability.

Dr. Ward agreed that radium for cancer of the fundus when used alone was not a safe procedure and he preferred to take the uterus out after radiation, but radiated first. The majority of carcinomas of the fundus require a diagnostic curettage to see if we are dealing with a polyp, and it is easy to place the radium at that time and then take out the uterus subsequently.

In 50 per cent of cases of carcinoma of the fundus, there is some reason why we cannot operate. They are old women, very often they have diabetes or cardiovascular disease, and are poor surgical risks.

Dr. Ward recommended the cautery with radium in all cases with an exuberant growth projecting into the vagina. He did not use the cautery in a case which was distinctly localized early in the cervix itself and had not attempted to do the Byrne operation of amputating the cervix.

Dr. Gordon asked why, with such brilliant results with radium alone, cases of the Wertheim operation and radium are reported. Those cases were all done in 1919 and 1920 when he first obtained the radium, and was feeling his way. In some of those early cases he used the radium and then the Wertheim afterwards, but since that time had not done any Wertheim operations but relied entirely on the radium. These cases, however, are not included in the radium statistics.

In answer to the remark about the five-year cure, the term is accepted by all men who are working with radiologic statistics. It simply means alive and symptom-free at the end of five years. By no means does it mean that the patient is permanently cured. Cases might be all right for five years and die later, 6, 7, 8, or 9 years, of carcinoma. Symptom-free means subjectively symptom-free, because many of these cases if examined show some infiltration, but the patient is symptom-free as far as she knows, well and able to do her work, with no gross evidence of disease apparent.

As to the use of needles, Dr. Ward believed he got some fistulae because the needles were too close together. Formerly he used 100 milligrams and 6 needles as the initial dose. He found it is much better not to put the needles closer than within 2 cm. of each other, therefore, in the average case he now uses 4 needles and 100 milligrams of radium unless the growth is very large when it will easily take 6 needles because of the excessive size of the cervix.

He did not fear spreading the disease by passing the anchoring suture through the cervix, as one does not hesitate to do a biopsy, which is an accepted procedure.

NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL
SOCIETY

MEETING OF APRIL 19, 1928

DR. E. L. KING read a paper entitled **Fetal Mortality in Breech Presentations. Is Prophylactic External Version Advisable?** (For original article, see page 78.)

DISCUSSION

DR. HILLIARD E. MILLER did not believe that a breech delivery should carry with it a higher mortality than other kinds. He said that even in cases of impacted shoulder, deep surgical anesthesia, preferably with ether, makes the procedure relatively simple, and the routine performance of episiotomy lessens the risk for the mother. By observing these few points, plus ironing out the vagina and waiting until the breech appears on the perineum before delivery is attempted, he has had uniformly good results in these cases. Good assistance is extremely important. If the membranes rupture early the insertion of a bag is the safest plan. It is well to remember that all manipulations must be extremely gentle, particularly when the hand is placed in the child's mouth, for fracture of the jaw is easily produced by the exercise of undue force.

Dr. Miller had no experience with prophylactic external version, because he saw no indication for its use, when breech delivery is so largely a simple and safe procedure.

DR. J. S. HEBERT said that the high fetal mortality in breech presentations, as shown by statistics collected by Dr. King, was a surprise to him. He would agree with Dr. Miller that the figures are frightfully high. With prophylactic external versions he had no experience except for a few cases so handled in the Charity Hospital. The results have not been satisfactory. Labor might be precipitated, severe hemorrhage from disturbed placental circulation or possibly malpositions may result, therefore he did not consider the operation advisable.

DR. KING (in closing) said some of the babies in his series were autopsied. They died of birth injuries, rupture of the adrenal, intracranial hemorrhage, etc. His figures are about the average as given in textbooks. His cases of primiparae showed a lower fetal mortality; this may be partly due to the fact that the obstetrician had time to get to the patient and render the necessary assistance. Some French writers advise no assistance until the shoulders and arms are delivered spontaneously. He believes that anesthesia is a great aid. Dr. King waits until the breech is on the perineum, then puts the patient to sleep and delivers the baby. He believes that we should teach that breech presentation is not easy to handle, and further that breech cases should be hospitalized, at least good assistance should be available, as one may be faced with a complicated operative delivery.

DR. LUCIEN A. LEDOUX read a paper entitled **Some Physiologic Aspects of Eclamptic Toxemia.** (For original article, see page 90.)

DISCUSSION

DR. H. VERNON SIMS remarked that Titus has recently shown that there is a hypoglycemia in eclampsia. A 25 per cent solution of glucose is given by him intravenously with the Stroganoff treatment. Labors are not terminated. All cases are handled in this way. Only one death is recorded.

Dr. Sims believes that after careful prenatal care, if the patient begins to develop symptoms, rigorous preeclamptic treatment should be started. If this does not help, the labor should be terminated.

DR. T. B. SELLERS has tried heparmone in four cases of preeclampsia, two were frank preeclamptics, two were nephritic toxemias. His results with heparmone in true eclampsia were quite gratifying, but the patients with nephritic toxemia were not benefited at all. He gave heparmone, two to four doses, in several cases just before labor started, but was unable to draw conclusions. Dr. Seller's experience with glucose in the treatment of pernicious vomiting of pregnancy has been that it is worthless unless given intravenously and he prefers to give small doses of insulin along with the glucose.

DR. J. S. HEBERT believes that the complicated chemical and functional alterations, characterizing the normal physiology of pregnancy, signifies the gradual adaptation to the exigencies created by pregnancy. In the constitutionally deficient woman, be it in organ or organ systems, adjustment is sluggish or possibly imperfect. Inadequate adjustment constitutes the pathologic physiology of pregnancy, expressed in a symptom complex and best described as the toxemias of pregnancy. Dr. Hebert believes that the underlying weak points are usually found in the gastrointestinal tract, the endocrine system, or in the cardiovascular renal system. He considers that Dr. Titus has given conclusive evidence that in eclampsia there actually exists a disturbed carbohydrate metabolism and that convulsive seizures occur at levels which can be designated as "relative hypoglycemia." There is a rise in blood sugar following convulsions, a natural physiologic response of the liver to muscular activity.

DR. E. L. KING mentioned the work Dr. R. C. Cross has been doing on liver function test in normal pregnancy. Dr. Cross finds that in normal pregnancy, the various liver function tests are always negative. In other cases with focal infections, etc., he has found a retention of dye showing a liver dysfunction and degeneration.

DR. LUCIEN A. LEDOUX (in closing) said that he had hoped that the discussion would be more along the lines of the subject presented.

The liver function test he considers a very valuable early or late diagnostic aid. He thinks it should be done immediately on the appearance of one or more symptoms or signs of toxemia, regardless of whether there are any blood pressure or urinary changes.

Dr. Ledoux believes that hypoglycemia when it does occur, is interpreted rather as an effect than as a cause, feeling that it results from a disturbed glycogenolytic function, resulting from the destruction of the liver cells, this occurring usually in the severe cases, where the damage to the liver is extensive.

CHICAGO GYNECOLOGICAL SOCIETY

STATED MEETING MARCH 16, 1928

DR. W. E. N. DORLAND demonstrated a specimen of the **So-called "Everting" Variety of Papillary Cystadenoma of the Ovary.**

DR. DORLAND removed tumors last October from a woman forty-nine years of age. She presented no symptoms whatever, but had visited her physician for the relief of an acute coryza. Not having seen her for a year, he made a complete examination and discovered a mass in the pelvis, with the presumptive diagnosis of cancer. Dr. Dorland found a nodular and irregular mass lying behind and to both sides of the uterus, fixed in its position and sensitive at spots, and made a diagnosis of probable carcinoma of the ovaries. Three days later he removed both ovaries. They were partially adherent to the uterus, but were readily detached and ligated. The pathologic examination showed bilateral papillomatous cystomas of the ovaries.

These growths are nonmalignant as regards metastasis by way of lymph-channels, but fragments of such tumors may be broken off and swept to any part of the peritoneum where they may adhere and develop into new papillomas, forming so-called "implantation" metastasis.

The everting variety of papillary cystadenoma of the ovary is much rarer than the inverting variety, in which the papillary excrescences are formed on the inner lining of the cyst and not on the outer surface. Because of the great tendency to form secondary implantation-growths on the pelvic peritoneum these everting cysts are very prone to recur, even when no implantation-growths can be detected at the time of operation. Recurrences are very apt to appear within two or three months after removal of the tumors. Six months after the operation, Dr. Dorland found the pelvis clear.

DR. A. H. CURTIS said that he and Dr. Watkins had had a patient with this type of growth in whom a recurrence did not appear until ten years subsequently.

DR. DAVID S. HILLIS reported a case of **Premature Separation of a Normally Implanted Placenta During Pregnancy.**

The case was presented because of the absence of the usual findings which enable one to make the diagnosis, and especially because of the lack of the board-like hardness of the uterus which is so often characteristic of this condition. Many obstetricians have insisted that this sign is often absent, but Dr. Hillis has found it so constantly present that he has come to depend upon it to differentiate premature separation from placenta previa.

Premature separation usually shows signs of shock which are out of proportion to the amount of external bleeding and usually out of proportion to the internal bleeding. The case reported showed absence of shock; the pulse was about 90. The uterus was rather doughy, but not hard. There was a small amount of bleeding externally. Fetal heart tones were absent. The case presented more of the usual findings of a placenta previa than those of a premature detachment of the placenta. It was only after vaginal examination showed that no placenta was in reach of the examining finger that the diagnosis was established in this case. The patient was delivered from below after induction of labor by a bag placed outside the membranes which were not ruptured at the insertion.

In a number of cases in the Cook County Hospital during the last fifteen years, Dr. Hillis managed practically all of them by means of a bag, with such success that he believes this should be the method of choice in the management of most of the cases of premature separation. The membranes are usually ruptured before the bag is inserted on account of the high intrauterine pressure; the patient goes into labor promptly, usually delivers spontaneously and the free use of pituitrin and the uterovaginal tamponade control the hemorrhage after delivery.

DR. CHARLES B. REED read a paper entitled, **Impetigo or Pyodermatitis Neonatorum**. (See page 49.)

DISCUSSION

DR. A. H. PARMELEE said he never knew there was such a thing as congenital impetigo until he started to work on the newborn service at the Cook County Hospital. Since then he had seen about five cases of what seemed to be undoubtedly congenital impetigo. He has not been able to recover any organisms from any of the pustules.

If it is true that this case of impetigo is of congenital origin it must be due to a blood stream infection.

Dr. Reed's paper stressed the idea that there was too much confusion in the various names applied to, what seems to be, one disease of varying intensity, the clinical manifestations depending upon the virulence of the organism and the immunity of the patient.

Aside from the aseptic technic which everyone admits is absolutely essential in handling newborn infants, particularly premature babies whose immunity against infection is invariably very low, trauma undoubtedly plays a large part in these infections. The pustules when they are only very infrequent in occurrence, usually appear at places where the skin is easily macerated. The baby's skin is very sensitive to any kind of irritation.

The problem of whether infected breast milk has anything to do with the situation seems to depend entirely on the question whether this infection is blood-borne or not. Before deciding whether congenital impetigo is due to an infectious organism more data must be at hand than are available at present. Practically all the cases of impetigo, pemphigus neonatorum, and Ritter's disease have in the past, given a culture of staphylococcus. If it is true that a hemolytic streptococcus was found in pustules on the scrotum of the baby reported in this paper, it is evident that there is a new situation to deal with and a wholly new attitude should be assumed toward the disease. Is it not possible that these blebs may be due to irritation rather than of an infectious origin?

DR. JAMES HERBERT MITCHELL said that several years ago, dermatology had been defined as a system of nomenclature. It is interesting to hear gynecologists talk about impetigo rather than pemphigus because dermatologists long have had the feeling that pemphigus neonatorum was impetigo. Dermatologists have a rather definite conception of pemphigus. There are three types which usually affect adults and are not seen in infants; they are not infectious, they are not contagious and they apparently have nothing in common with this neonatorum type. In dermatology three types of impetigo are recognized. One is the impetigo of Tilbury Fox, now generally recognized as due to a streptococcus. He was interested to hear that a streptococcus is rarely found in the newborn; it is common in children and adults. This is a superficial type of large bullous lesions having a very thin wall and rupturing early, leaving nothing more than an erosion upon which the healed up

crust develops. Then there is the impetigo of Bockhart which is due to the staphylococcus and which forms a little white drop of pus. Then there is impetigo vulgaris, a combination of the two. Oftentimes the streptococcus is there but is overgrown by staphylococcus, and staining agents such as violet green will be necessary to inhibit the staphylococcus. Then there is pyoderma which is known as ecthyma which is likely to occur under the poorest of hygienic conditions or in much debilitated individuals. He is inclined to believe that the streptococcus will be found very much more often than it seems to have been in gynecologic and obstetric work if this causative agent is borne in mind.

The mode of infection interested him because several years ago he showed two cases that puzzled him very much. The infant was born, developed impetigo and there was no possible explanation for this contagion. In spite of everything the child died. Two years ago, the mother gave birth to another child and it likewise died, after which it was found that this mother had a streptococcal focus of infection in the birth canal and in both cases the infection occurred on the scalp, probably during passage.

As regards treatment, oftentimes ointments are not of much value but in the few cases of infant impetigo that he had occasion to treat, complete potassium permanganate baths have proved to be very beneficial. They are easily carried out, are not irritating, and are much more effective than ammoniated mercury.

DR. SYDNEY S. SCHOCHET said it was unfortunate and confusing to have the different phases of the same lesion classified as separate entities. Dr. Reed has given us a very clear analysis of this lesion and broken down the traditional classification.

We can appreciate this new classification if we review the history of these lesions. During the middle of the past century the etiologic factors were considered as systemic and later, through the researches of Hebra and others, were grouped under external causes. At present we believe that the etiologic factors are due to external and internal conditions, such as the metabolic disturbances. In other words, we are accustomed to thinking in terms of gross lesions in the body rather than deranged physiologic function without actual gross lesions and histopathologic changes. A good example of this is found in dermatitis, one of the common lesions in the skin in which we find a degeneration of connective tissue with infiltration. The dermatologist, the pediatrician and clinician do not agree as to etiology. There is no reason that one and the same cause may not give rise to many different clinical manifestations or that the same clinical manifestation may not be the result of many etiologic factors. For this reason we have different clinical names for different phases of the same lesion.

One of the questions suggested by Dr. Reed was whether the staphylococcus is changing its virulence. There is one other factor we should bear in mind; namely, bacteriophage. Most organisms have a substance which we speak of as bacteriophage. It is associated with almost all bacteria, passes through the filter and produces typical lesions.

Toxic substances may also produce lesions of the skin and it may be due to these causes rather than congenital infections.

DR. FRED FALLS had never seen epidemics of so-called impetigo contagiosa in the newborn. All the lesions that have been seen were superficial. He has seen other suppurative lesions apparently give rise to pemphigoid lesions. In one case a breast abscess occurred in a newborn child. This breast abscess followed the demonstration by one of the instructors of "hexen-milch" in the baby. The next day it developed a breast abscess in which the staphylococcus was found. In twenty-

four hours a typical pemphigus lesion occurred about two inches from the breast, from which staphylococcus was recovered. As far as the organism itself is concerned, in the lesions he has studied, staphylococcus has always been recovered and it has been seen in the smears as well as in the cultures. He has never seen a typical streptococcus in the smears or been able to culture it. This may be due to a faulty technic but so far as he knows no one has been able to recover streptococcus from pemphigus and fulfill the four laws of Koch that must be fulfilled before an organism can be considered the cause of a disease. This he has accomplished with the staphylococcus, making a culture from a typical lesion, growing it in broth and injecting it into his own arm and producing a typical lesion and recovering from it the staphylococcus in smears and in pure cultures.

Concerning the question of whether there are different varieties of staphylococci concerned, and whether they are the same from a pustular lesion, nonpemphigus in nature, he took the various culture media and ran pemphigus staphylococcus and staphylococcus from a boil through milk gelatin, blood agar broth and various sugars, titrated the acid formation, and tried to differentiate between the two organisms. They were always the same and were so nearly alike that one could not distinguish which was from the boil and which was from pemphigus. The organism recovered was tested as to virulence by injecting into guinea pigs, with negative results. He has seen several breast abscesses arise in mothers who were suckling babies who had pemphigus neonatorum. He has one patient who demonstrated the potential virulence of the organism in which the baby developed pemphigus and the mother developed breast abscess, that did not suppurate. After leaving the hospital she developed a felon on her thumb and died. Staphylococcus was recovered from the felon.

The source of infection has already been brought up by Dr. Reed, that is, contamination from the various personnel. One epidemic at Cook County Hospital was traced to one of the night workers who had a bad acne. As soon as she left the hospital the epidemic ceased. A small epidemic of pemphigus was started in Iowa that was traced to an intern who was on duty while he had a pustular lesion on the neck. Another small epidemic was traced to the fact that undisinfected containers were used to take the linens back to the wards from the laundry. After that was stopped there was no more pemphigus.

It has been his experience that by rupturing the lesion under alcohol and putting on two per cent ammoniated mercury with prompt isolation of the case, the epidemic had been aborted.

Dr. Reed's statement of the length of time it took the lesions to appear on auto-inoculation was incorrect. Dr. Falls injected the organism by taking a needle, dipping it into the culture and injecting it into his arm at about four o'clock in the afternoon and the next morning he had a very nice bleb which was typical and which was without irritation. He simply put the needle under the stratum corneum of the skin where apparently the lesion arises. A control using sterile salt solution was made.

As far as the lesions are concerned which are seen at birth, Dr. Falls did not venture to say to what they were due but he would hesitate to accept the theory that they are organisms that come through the placenta and through to the blood stream and produce the pustular lesions on the baby. Theoretically one would expect more of a severe inflammatory process than the relatively minor disturbances that one sees in these neonatorum lesions.

DR. REED, in closing, said Dr. Falls brought up a very interesting statement regarding the subject of water. Dr. Reed sent out 250 questionnaires and only two or three admitted any contaminations in their maternities since the disturbance in

1917. The condition was so universal that it could hardly be attributed to Chicago water. It is far more probable that the immunity has been diminished by the excess of carbon monoxide from the innumerable motor exhausts.

DR. CHARLES EDWIN GALLOWAY, by invitation, presented a paper entitled, **Anemia in Pregnancy**. (See page 84.)

DISCUSSION

DR. W. C. DANFORTH said that as anemia occurs so frequently in pregnancy some attempt at correcting seemed worth while in as much as some other complication, such as postpartum hemorrhage, would be more serious in a woman who is already anemic.

Treatment during pregnancy is only relatively efficient. Many respond poorly but in some a fair degree of relief may be obtained by oral and intramuscular use of iron or by heliotherapy. The value of the lamp which is at present used in light therapy is not definitely established. It is quite possible that the lamp after being used for some time is not of the same efficiency as at first owing to changes in the glass.

DR. J. P. GREENHILL said that this paper deals essentially with secondary anemia. He also has something to say about pernicious anemia of pregnancy and refers to the fact that it is very uncommon during pregnancy. This holds true for the European countries and the United States but in India a form of pernicious anemia is very common during gestation. Some years ago, Dr. Greene-Armytage, professor of Obstetrics and Gynecology in Calcutta stated that pernicious anemia was frequently encountered in Calcutta. Last year in the *Indian Medical Gazette* there were two papers dealing with anemia during pregnancy. One of the authors analyzed over 400 cases and he believed the cause of the anemia is a toxemia. The other author who reviewed 150 cases is of the opinion that concealed syphilis was responsible for a large number of cases.

DR. C. S. BACON asked how the hemoglobin determinations were made, feeling that the ordinary methods were pretty well discredited. He did not hear any reference to the use of liver in the treatment. Williamson of this city produced secondary anemia in various ways in animals and concluded that the administration of iron in any form, by mouth or hypodermically or intravenously was absolutely without result.

DR. GALLOWAY, in closing, said that there seems to be a fairly close relation between so-called pernicious anemia and certain cases of toxemia of pregnancy. Perhaps some of the cases reported from the Orient might be of toxic origin. The majority of these cases did not have any prenatal care and that practically all the women were seen for the first time in the last few weeks of pregnancy, at term or soon after term. There were no women who would be under the care of physicians. Practically everyone that he could get specific data on were cases that had been very much neglected. He did not run across any animal experiments in pregnancy anemia in the English or German literature.

The hemoglobin estimations were made by the modified Sahli. Some of them were made with the Dare. He told some of the patients to eat liver as he was not afraid of having the pregnant woman eat liver or take a certain amount of meat and wondered whether meat plays a very important part in the toxemia of pregnancy.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

The Hormones of Ovary and Anterior Pituitary

Bugbee and Simond: The Effects of Injections of Ovarian Follicular Hormone on Body Growth and Sexual Development of Male and Female Rats. *Endocrinology*, 1926, x, 360.

Bugbee and Simond experimented with ovarian follicular hormone to determine its effect on bodily functions and to note whether or not it would stimulate body growth and cause a precocious sexual maturity in young female rats. Both male and female rats were used so as to determine whether or not the female hormone exerts any effect on normal or castrated males.

Their conclusions might be briefly summarized as follows:

Castration causes both female and male rats to grow heavier. Subcutaneous injections of ovarian follicular hormone induces loss of weight both in normal and castrated female and male rats. These injections do not cause male or female rats to reproduce earlier.

Ovarian follicular hormone is not an entirely specific female hormone, for it reduces the weight of male rats in the same way as it reduces the weight of female rats. Therefore, the conclusion can be drawn that the follicular hormone does not necessarily have any antagonistic effect on the male sexual apparatus.

W. KERWIN.

Terada, M.: The Changes in the Ovaries and Other Organs of Animals Injected With Various Ovarian Substances. *Japan Medical World*, 1927, vii, 233.

Autolysates of corpus luteum, interstitial gland, and follicular fluid when injected intraperitoneally into white rats, produce an hyperemia and degeneration of the ovaries. The interstitial gland is the first to degenerate, and the follicles are second. The germinal epithelium, lutein cells, and the very young follicles are but slightly affected. A true cystic degeneration of the follicles was invariably produced. The follicular fluid invades the interstitial gland most markedly and this tissue shows the least resistance. The ovaries of very young animals are more resistant than are those of older and matured animals. These ovarian tissue autolysates also caused a certain amount of degeneration of the kidneys, probably on account of the toxic effect produced on the kidneys.

RALPH A. REIS.

Trivino, F. G.: Increased Uterine Development by Means of Serum From Pregnant Women. *Klinische Wochenschrift*, 1926, v, 2022.

The author injected serum from pregnant women into young, immature white mice. In 42 of the 43 thus injected, there was found, one week later, a marked hypertrophy and maturation of the uterus. Sections through the musculature

showed no changes, but the mucosa invariably showed a full adult development even though the mice used were very young. The uterine lumen had always reached adult size. On the other hand, carefully carried out control experiments, using serum from nonpregnant women, showed no such changes in uterine structure or development. This pregnancy serum proved to be thermostabile, soluble in alcohol, and was dialyzable.

On account of the large amount of this hormone present in the blood serum of all pregnant women, the author cannot concede that the ovaries alone could or do produce it. He is definitely of the opinion that both the placenta and the uterine wall contribute toward the production of this pregnancy hormone as well as the ovaries.

RALPH A. REIS.

Dohrn, M., Faure, W., Poll, H., and Blotevogel, W.: Tokoinine, Vegetable Substances With Activity Resembling Sex Hormones. *Medizinsche Klinik*, 1926, xxii, 1417.

Biologic observation shows that with increased knowledge the physiologic-chemical boundaries between animals and plants become less and less distinct. The authors have shown that substances having the action of sexual hormones are not limited to the sexual organs of animals. With vegetable substances they have produced in mice the typical epithelial changes in the vagina as described by Stockard and Papanicolaou. They derived their material from sugar beet root, potato bulbs, parsley roots, cherries, plums, and yeast. The raw extract is similar to the sex hormones obtained from the placenta or ovary, and is an oil. The authors found that this substance produced an increased growth of uteri in four days.

J. P. GREENHILL.

Smith, Margaret, G.: A Study of the Ovarian Follicular Hormone in the Blood of the Pregnant Woman. *Bulletin of Johns Hopkins Hospital*, 1927, xli, 62.

The concentration of a substance, identical in its biologic property with the ovarian follicular hormone, increases in the blood of pregnant women from the onset to the termination of pregnancy. It has always been found in the same concentration during and shortly before labor, and its concentration at this time is greater than that found at any other time.

There is an immediate rapid disappearance of this substance from the blood following delivery. It can be demonstrated in the urine before and following labor.

The amount found in the placenta per gram of weight is approximately twice that found in the blood per cubic centimeter.

The concentration in the maternal blood during labor and in the blood from the cord is the same.

C. O. MALAND.

Hirsch, H.: Variations in the Female Sex Hormone Content in the Blood of Women. *Archiv für Gynäkologie*, 1928, cxxxi, 172.

The amount of female sex hormone in the blood of normal and healthy women increases during the normal intermenstrual period and reaches its peak the day before the menstrual flow begins. It decreases in amount gradually during the days of the menstrual flow. Menstrual blood contains from three to six times as much female sex hormone as does the circulating blood. There is a steady increase in the amount of this hormone during pregnancy up until delivery. In the days immediately following delivery it decreases rapidly until the twelfth day postpartum, at which time it can no longer be recovered from the blood.

RALPH A. REIS.

Dohrn, M., and Faure, W.: The Excretion of the Female Sex Hormone. *Klinische Wochenschrift*, 1927, vii, 943.

It is a well-established fact that the female sex hormone is excreted in the urine of adult males as well as adult females. The amount excreted in the urine of pregnant women is very large, namely, one thousand mouse units per liter. The authors found a comparatively tremendous excretion of the female sex hormone—thirty thousand mouse units per kilogram—in the dried feces of pregnant women.

RALPH A. REIS.

Zondek, B.: Female Sex Hormone in the Urine, Especially in Pregnant Women. *Archiv für Gynäkologie*, 1928, cxxx, 485.

The author describes his method of extracting the female sex hormone from the urine. The lipoids are first extracted from the urine without the use of alcohol. The residue is then alkalinized and heated, dissolved in water, and shaken up with ether. The latter is then removed and the new residue dissolved in distilled water or weak acetic acid solution and heated. This latter mixture is filtered, and the female sex hormone is contained in the filtrate which should be colorless, odorless, and clear.

RALPH A. REIS.

Zondek, B., and Aschheim, S.: Anterior Lobe of the Pituitary. *Archiv für Gynäkologie*, 1927, cxxx, 1.

The authors implanted various endocrine glands and injected different body fluids into castrated female mice but failed to establish estrus. They believe, therefore, that the ovarian hormone is produced only by the ovary, with the possible exception of the placenta. The feeding of human thymus does not inhibit ovulation, neither does the removal of both adrenal bodies. They were also unable to establish sexual function in immature female mice by feeding or transplanting pieces of the thyroid, thymus, pineal body, adrenals, testes, or posterior lobe of the pituitary. A transplant of the anterior lobe of hypophysis, either human or animal, however, produced estrus in from eighty to one hundred hours. The gland from a male subject was as effective as that of a female subject. This hormone or activating substance is still present in women who have passed the menopause. It appears to be the motor of the sexual function. It stimulates follicular function, ripens the follicles, and mobilizes the ovarian hormone. This latter has a specific action on uterus and vagina.

RALPH A. REIS.

Zondek, B., and Aschheim, S.: The Hormone of the Anterior Lobe of the Hypophysis. *Klinische Wochenschrift*, 1927, vi, 249.

From their experiments on mice, the authors find that ovarian function cannot be established by nonspecific stimulation, even if endocrine in origin, except by transplantation of the anterior lobe of the hypophysis. The posterior lobe is inactive in this respect. This hormone of the anterior lobe is the same in mice as in the human being. In human beings it is found in both men and women. It is thus established that one endocrine gland—the ovary—is dependent upon another endocrine gland—the anterior lobe of the hypophysis—for its stimulation and activity.

Sections of young and immature ovaries stimulated to an hyper-development and functional activity by means of anterior lobe transplants show a marked development of the follicular apparatus and of corpus luteum development.

They conclude from their extensive experiments that the anterior lobe of the hypophysis is the motor of the sexual functions and that the ovarian hormone

plays only a secondary rôle. The ovum plays only a very minor part, for roentgen destruction of the ova does not prevent hormone formation for many weeks. It stops completely only if sufficient radiation is used to prevent the anterior lobe hormone from stimulating the follicles to ovarian hormone formation.

RALPH A. REIS.

Aschheim, S.: Hormone and Pregnancy. Medizinische Klinik, 1926, xxii, 2023.

The author discusses his studies on the ovarian and hypophyseal hormones. During pregnancy the anterior lobe of the hypophysis is definitely enlarged, and this is essentially due to proliferation of the chief cells. The eosinophilic and basophilic cells regress. In the ovary the changes which take place during pregnancy are as follows: Maturation of follicles ceases. The corpus luteum persists until the end of pregnancy and is distinguishable from the corpus luteum of nonpregnant women by the absence of sudanophile lipoids, by the presence of colloid between the cells, and by the appearance of masses of calcium. The cortex of the ovary also shows changes during pregnancy. Many follicles become atretic which results in a marked increase and hypertrophy of the theca interna cells.

With Zondek the author has been able to isolate ovarian and anterior hypophyseal hormones. The test object for the ovarian hormone was the vaginal epithelium of the mouse, and the test object for the hormone from the anterior lobe of the hypophysis was the ovaries of infantile mice. The author found the ovarian hormone during pregnancy in the following organs: (1) the corpus luteum (in half the cases); (2) the cortex of the ovary (in one-third of the cases); (3) the placenta (always); (4) in the maternal blood from the end of the fourth month; (5) in the blood of the umbilical cord. The hormone was not found in the decidua or in the liquor amnii.

During pregnancy a substance identical with the hypophyseal hormone was found in the decidua, in the corpus luteum, in the placenta, in the maternal blood, especially after the fourth month, and in the blood of the umbilical cord.

The hormones of both the ovary and the anterior lobe of the hypophysis are so greatly increased during pregnancy that their presence in the maternal blood can be demonstrated by the injection of a small amount of serum. Both hormones stimulate growth. The ovarian hormone stimulates the genital tract while the hypophyseal hormone affects the entire body.

J. P. GREENHILL.

Zondek, B.: The Hormone of the Ovary and the Anterior Lobe of the Hypophysis. Medizinische Klinik, 1927, xxiii, 463.

The author, together with Aschheim, definitely proved that the changes in the vaginal epithelium and vaginal secretion are indicative of the activity of the ovarian hormone alone. Zondek found that the only source of the ovarian hormone is in the follicular apparatus of the ovary, that there is a cyclic production of hormone and that the quantity varies in this cycle. The hormone is produced by both theca and granulosa cells. He succeeded in separating the hormone from the lipid with which it is bound and has prepared an aqueous solution of the hormone which is being marketed under the name of Folliculin. The latter produces the same results as follicle fluid. Furthermore, implantation of human corpora lutea produces the same effect as folliculin. By means of the latter many amenorrheic women were made to menstruate, but these were selected cases where ovarian dysfunction was thought to be the cause of the amenorrhea. Folliculin has seemed to help not only the menstrual disorders but also secondary sex characters and sterility.

The ovarian hormone is produced only in the ovary, except in pregnancy when

it is formed also in the corpus luteum of pregnancy, in the atretic follicles which are rich in theca cells, in the blood, and perhaps also in the placenta.

The author's researches led him to the discovery of a new hormone. All kinds of substances and glands were tried in an effort to stimulate ovarian function and all but one failed. This exception was the anterior lobe of the hypophysis, for when this was implanted in an infantile mouse, the latter went into typical heat after ninety-six hours. The anterior lobe of the hypophysis, therefore, is the motor of the ovarian function. It does not matter whether the hypophysis is from a human being or from an animal, or from male or female. While it is true that both ovarian and hypophyseal hormones produce heat in animals, these hormones are by no means identical. The hypophyseal hormone is effective only when an animal has ovaries, because it produces its effect through the ovaries. It brings about a ripening of the follicle and ovum and the formation of a corpus luteum. The test object for the ovarian hormone is the vagina of a castrated mouse while the test object for the hypophyseal hormone is the vagina and, especially the ovaries, of a noncastrated, infantile mouse.

J. P. GREENHILL.

Aschheim, B., and Zondek, B.: Hormones of the Anterior Lobe of the Pituitary and of the Ovary in the Urine of Pregnant Women. *Klinische Wochenschrift*, 1927, vi, 1322.

The authors found one or more mouse units of ovarian hormone per cubic centimeter of urine excreted by pregnant women. This hormone appears in the urine during the fifth month of pregnancy and later in quantities sufficient to activate white female mice before maturity. The hormone of the anterior lobe of the pituitary is found in the urine much earlier, i.e., about five weeks after the last menstruation. The authors suggest a new method of early diagnosis of pregnancy by means of the finding of this hormone in the urine.

RALPH A. REIS.

Liebesny, P.: The Pituitary Gland and the Central Regulation of the Gonads. *Klinische Wochenschrift*, 1927, vi, 52.

Patients suffering from a primary insufficiency of the sexual glands all showed a lowered basal metabolic rate. When these patients were subjected to Doppler's "chemical sympathetectomy" or to diathermy of the sexual glands and such treatments were successful, the basal metabolism improved. When the specific dynamic action of proteins was very low, together with a gonadal hypofunction, there was often improvement following careful and extensive diathermy of the pituitary region. It is probable, however, that this improvement was due to stimulation of the brain centers themselves rather than to stimulation of the pituitary gland.

RALPH A. REIS.

Aschheim, B., and Zondek, B.: Pregnancy Test. *Klinische Wochenschrift*, 1928, vii, 8.

The authors' test consists in injecting from one to two cubic centimeters of the morning urine from pregnant women into young female mice and noting the effect upon the ovaries. Castrated adult mice are used as controls. The authors have previously reported the finding of the female sex hormone in the urine of pregnant women, and such urine when injected into immature female mice stimulates the ovaries. In this series the test was used 78 times and was unquestionably positive in 76. A repeat test of the remaining two gave a positive reaction on one. By this method pregnancy can be diagnosed within five days after the first missed menstrual period.

In 236 controls, there was a weakly positive reaction in three cases of myxedema and acromegaly, in 20 per cent of the cases of genital carcinoma, and in 2 persons, 1 man and 1 woman, with neither an endocrine disturbance nor a malignancy.

RALPH A. REIS.

Frank, Robert T., and Goldberger, M.: Clinical Data Obtained With the Female Hormone Blood Test. *Journal of American Medical Association*, 1928, xc, 106.

This report is based on and represents the outgrowth of all of the work of Frank and his collaborators on the female sex hormone. He summarizes his investigations since 1917 and reports further observations on the presence and concentration of the female sex hormone in the circulating blood of the human female by means of the reaction which he published in detail in 1926. In a large number of tests he again is able to demonstrate that the female sex hormone concentration in the blood increases after ovulation up to the time of menstruation. With the onset of the flow the hormone disappears from the circulating blood. The hormone is found in great concentration in the menstrual as well as in the postpartum blood. It is found in the circulating blood from the twelfth to the fortieth week of gestation.

The blood of many women suffering from menstrual abnormalities was studied. Six cases of menorrhagias showed high hormone concentration in the blood preceding menstruation. Metrorrhagias (16 cases) could be divided into two groups, the one revealing the typical hormone concentration cycle, the other showing no hormone in the circulating blood at any time. Women with marked premenstrual tension (nervousness, unbalanced autonomic system, psychic changes) exhibited an excess of hormone in the blood.

A certain number of patients with amenorrhea showed absence of hormone, while in a few other patients the hormone appeared in four weekly intervals in demonstrable quantities. This latter group seems to carry a more favorable prognosis.

In 4 persons with absent vaginas the attempt was made to determine the sex with this test. In 3 of them repeatedly the female sex hormone could be demonstrated in the blood, and even the typical cyclic change in quantity.

Sterilities seemingly fall into two classes. In the one the typical hormone concentration cycle is evident, in the other ovarian function is distinctly depressed. The number of cases so far studied is too small to draw conclusions.

By this same test these investigators were able to determine the death of the fetus after the twelfth week. With termination of pregnancy the hormone disappears quickly from the circulating blood.

This article contains many valuable references to literature and a detailed description of the technic elaborated by Frank.

GROVER LIESE.

Dohn, M.: Is the Allen Doisy Test Specific for the Female Sex Hormone? *Klinische Wochenschrift*, 1927, vi, 359.

The author made Allen Doisy tests with testicular extracts and obtained the same results as with ovarian extracts, i.e., a definite cornification of the vaginal epithelium. He, therefore, cannot agree with Allen and Doisy, or Stockard and others who believe the test to be specific.

RALPH A. REIS.

Laqueur, E. et al.: The Presence of the Female Sex Hormone in the Urine of Men. *Klinische Wochenschrift*, 1927, vi, 1859.

The authors review their previous work with the female sex hormone and report here the fact that the identical hormone, as to composition and action, can be

recovered from the urine of sexually potent and healthy men. There is still a question as to the structure of these hormones but certainly their function is identical in producing estrus in the rat and in producing uterine overgrowth in immature rats. The hormone is found in comparatively large quantities in the urine.

RALPH A. REIS.

Schenk: Changes in the Hypophysis of the Rat After Operative and X-ray Castration. *Zeitschrift für Geburtshilfe und Gynäkologie*, 1927, xci, 483.

During pregnancy in human beings and most suckling animals an enlargement of the anterior lobe of the hypophysis takes place. At the same time acromegalic changes occur, accompanied by enlargement of some joints, especially those of the spine. The majority of investigators say that the enlargement of the gland is due to an increase in the number of the eosinophilic cells; some that it is due to an increase in size and number of chromaffin cells, and others to basophilic cells. The enlargement has been confirmed by so many that there can be no question of it.

Most investigators find an enlargement as well after castration. Tandler x-rayed eunuchs and showed an enlarged cella tureica. Zacherl described a vacuolated cell having a large, vesicular central nucleus which Biedl considered to be the end stage in the development of the eosinophilic cell. Addison and Nukariya found large basophilic cells which the latter thought were not formed from eosinophiles. The same change was found whether the castration was done before or after sexual maturity.

The author repeated these experiments on rabbits, cats, and rats by castrating some and treating the testicles of others by x-ray. He found new cells in the hypophysis which he called castration cells. They were large, had distinct edges, stained weakly and, as they grew older, showed a vacuolated appearance with the nucleus excentrically placed, so that they finally appeared like signet rings.

These same changes took place in the hypophyses of the animals treated with x-ray but at a slower rate.

It can be said in the light of these and earlier experiments that there is a relationship between the sexual glands and the hypophysis, as shown by the examination of the hypophysis in pregnancy in human beings and also in lower mammals.

Changes in the hypophysis after castration are not found as generally and typically as one would think from the literature on the subject. Also the changes that do take place are in another direction than most authors think. The changes are characteristic in the rat but not so in the rabbit and were not constantly found in the cat.

FRANK A. PEMBERTON.

Aschheim, S., and Zondek, B.: Ovum and Hormone. *Klinische Wochenschrift*, 1927, vi, 1321.

The authors destroyed the process of ovulation in white mice by means of roentgen rays. Normal estrus followed, so that the ovum cannot be the origin of the ovarian hormone. Injections of this ovarian hormone into young and immature white mice produced estrus without any maturation of the graafian follicles. The ovarian hormone, therefore, does not influence the process of ovulation. Estrus appears in such animals in one hundred hours or less, if extracts of the anterior lobe of the pituitary gland are injected. The authors conclude that the ovum, ovulation, and the ovarian hormone are all dominated or controlled by the hormone of the anterior lobe of the pituitary gland.

RALPH A. REIS.

Westman, A.: The Primacy of the Egg Cell. *Acta Obstetrica et Gynecologica Scandinavica*, 1928, viii, 166.

The author performed bilateral salpingectomy on rabbits about twenty-four hours after coitus, when all the ova were situated in the tubes on their transit to the uterus. By doing this he eliminated all influence on the animals that could be excited by the ova cast off at the time of follicular rupture. In spite of these operations, the corpora lutea as well as the uterine endometrium passed through exactly the same cyclical changes as those found in pseudopregnancy. The experiments indicate that the development and function of the corpus luteum are not dependent upon products of absorption from ova liberated from the follicles.

J. P. GREENHILL.

Ancl, P., and Bouin, P.: Concerning the Biologic Action of the Corpus Luteum. *Gynécologie et Obstétrique*, 1926, xiii, 401.

The authors disagree with Schiekele's hypothesis that it is the follicle which conditions the modifications of the uterine mucosa in the preparation for nidation and that the corpus luteum only prolongs this state. The authors studied these changes in the rabbit and conclude that all the structural transformations which are manifest in the uterine cornua present a constant chronologic relation with the evolution of the corpus luteum. These same structural transformations are strictly identical with those which occur in the uterus of fecund females and precede the fixation of the ovum. There exists between the ovarian and uterine changes, not only a constant chronologic relation but a relation of cause and effect. If one destroys the corpus luteum following coitus with the fine point of a galvanic cautery, the process is interrupted immediately, and the mucosa returns to its normal reposing state. This does not occur if the ovary is similarly injured elsewhere. It is not the follicle which determines these changes, because at the time at which the follicle is at the height of activity proliferation of the mucosa never takes place before the formation of the corpus luteum. To suppose that the corpus luteum does not determine this preparation but merely assumes a "protective rôle" is to deny the strict determinism of biologic phenomenon. Schiekele's chief postulate is based on the fact that ovulation may occur as late as the twenty-third or twenty-fourth day of the menstrual cycle, and yet the endometrium be apparently at the height of its development as evidenced by the normal sequence of menstruation. Under such conditions, according to Schiekele, it is only the follicular apparatus which could have determined the hyperplasia of the mucosa, for the corpus luteum could not have been sufficiently formed to incite the changes of hemorrhage, exfoliation, etc. The authors point out that in the normal course of events as soon as the follicle is ruptured, the corpus luteum forms and the uterus undergoes the characteristic preparation. This preparation requires, to become complete, the time which is indispensable to the ovum to arrive at its place of fixation. The endometrial slough in such an event comes not at the period of maximum development of the mucosa but before, and is merely an abnormality, and the function of a non-physiologic course of events. In other words, under certain abnormal or pathologic conditions, the uterus is able to react by a bloody discharge due to corpus luteum action before the complete preparation of the mucosa for nidation.

GOODRICH C. SCHAUFFLER.

Uhlmann, F.: Is there a Hormonal Influence on Sex? *Medizinische Klinik*, 1928, xxiv, 1088.

The old belief was that sex is determined at the very latest when fertilization takes place and that the sex cannot be affected after fertilization has taken place.

If this belief is accepted, some facts are hard to explain. For example, among amphibians and lower animals the sex of the embryos may be affected by changing the temperature of the environment. The author reasons that if the sexual organs of fully mature animals can be affected by the sex hormones, it should be simple to influence the sex of a developing fetus. He, therefore, injected ovarian hormone into rabbits and then permitted them to mate. He found that the sex was affected in utero, for the offspring showed an overwhelming number of females. Fellner obtained the same results.

J. P. GREENHILL.

Heyn, A.: The Influence of Ovarian Function on the Basal Metabolism. *Archiv für Gynäkologie*, 1927, cxxix, 760.

The author studied the basal metabolism in 100 women and found that the normal menstrual cycle in healthy women has no effect upon metabolism. Dysmenorrhea likewise produces no changes. Severe ovarian insufficiency (primary amenorrhea) shows a decrease of more than 10 per cent in the metabolic rate. There is an increase of more than 10 per cent in about one quarter of the patients suffering from hemorrhagic metropathies and an increase of from 10 to 20 per cent in about one-half of the patients suffering from myomas. Castration produces a temporary decrease in the metabolic rate for from about three to six months in about one-half of the patients but in nine months the metabolic rate is again normal.

The results during and following normal menopause vary from 10 plus to 10 minus, and are inconclusive. The administration of ovarian extracts to menopausal patients, showing a decreased metabolic rate, invariably increases the rate to normal but never increases the rate above normal. The ovaries, therefore, have no direct effect upon metabolism but only a slight and secondary effect indirectly by virtue of the effect which the ovaries exert upon the thyroid. Amenorrhea is not the effect of ovarian insufficiency but rather of the insufficiency of the entire endocrine system.

RALPH A. REIS.

Schultze, G. K. F.: Ovarian Function, Potassium and Calcium Ion-Concentration of the Blood Serum and the Vegetative System. *Archiv für Gynäkologie*, 1925, cxxvi, 35.

Schultze finds a definite relationship between ovarian function and the potassium-calcium concentration in the blood serum, which suggests some influence of the corpus luteum on the vegetative or sympathetic nervous system. When there is a deficiency of corpus luteum stimulation, there is an overstimulation and predominance of vagus tonus. In some of these patients the potassium was as low as 14 milligrams per 100 c.c., although the calcium content was seldom increased. The author believes that this lowered concentration in the blood serum speaks for an increased concentration in the tissues.

RALPH A. REIS.

Vogt, E.: Insulin and Ovarian Function. *Zentralblatt für Gynäkologie*, 1927, li, 719.

Summarizing the results of his experiments the writer states that insulin has various effects upon organs, organ-systems, and metabolism. In the diabetic patient it influences the carbohydrate metabolism. Undoubtedly this is its essential effect. In the nondiabetic individual it can influence metabolism, in general causing obesity, or the endocrine system.

Insulin also has an effect on the internal secretion of the ovaries during menstruation and changes the irritability of the vegetative nervous system, which depends largely upon the calcium-contents of the blood. It reduces menstrual hyperglycemia as well as amount and duration of the flow. Hemorrhages due to a dysfunction of the ovaries, especially those of puberty and climacterium, are favorably influenced with insulin. Two injections of from 20 to 30 units daily before noon and evening meal, over a period of three or four days, are sufficient to obtain a beneficial effect.

GROVER LIESE.

Vogt, E.: Hormonal Sterilization of Female Animals With Insulin. *Medizinische Klinik*, 1927, xxiii, 557.

For purposes of sterilization there are three procedures: namely, operation, radiation, and hormonal therapy. Operation and radiation have certain disadvantages, and sterilization by means of hormones is still in the experimental stage. A number of individuals have produced sterility by means of the injection of sperm. Others accomplished this end by transplanting ovaries from gravid animals, by injecting ovarian extracts from pregnant animals, and by means of placental extracts. Likewise extracts from the corpora lutea of pregnant and nonpregnant cows produced sterility in rats. Vogt made rabbits sterile by injecting insulin. This is additional proof of the close relationship between the pancreas and the ovaries. Hormonal sterilization, according to the author, is the ideal method, because it is simple, certain, and safe.

J. P. GREENHILL.

Vogt, E.: The Dependence of Insulin Effect on the Ovary. *Deutsche medizinische Wochenschrift*, 1928, liv, 701.

Interrelation of the various hormones is discussed in the particular case of insulin to ovary. The author had previously used insulin in the treatment of uterine hemorrhages and for increasing the weight of patients in a subnormal state of nutrition. On these occasions he found that the effect of insulin on the same patient was quantitatively varying according to the period of the menstrual cycle. Experiments were carried out on healthy women, who were injected with a constant dose of insulin shortly before menstruation, and in the first and second part of the intermenstruum. The fasting blood sugar before and after the injection was determined and compared. In 50 women a regular change in the insulin reaction was found. Insulin was most effective immediately before menstruation. Its efficiency was decreased after the menstruation and increased again beginning with the middle of the intermenstrual period.

The same experiment on 60 pregnant women showed the effect of insulin considerably more constant, especially during the second half of pregnancy. This seemingly further supports the author's assumption, since the follicular cycle of the ovary is arrested during pregnancy. Other experiments were made with insulin activated with serum obtained from women in the different stages of the menstrual cycle. The results confirmed the previous findings: serum taken from women immediately before menstruation activated insulin most markedly; serum from women castrated by x-ray or operation, was the least effective.

GRUENFELD.

Haberlandt, L.: Hormonal Sterilization of Female Animals. Zentralblatt fuer Gynakologie, 1927, li, 1418.

Since 1919 Haberlandt is experimenting on the problem of producing temporary sterility in female animals. Subcutaneous transplantation of ovaries from pregnant rabbits and guinea pigs into nonpregnant animals produced temporary sterility in these. The effect is thought to be brought on by the formation of a hormone in the transplanted corpus luteum, which inhibits follicle maturation. After reabsorption of the transplanted ovaries the animals became pregnant and gave birth to mature, normally developed, living young. Sterility could be attained for 2 to 3 months.

Identical results were obtained by Haberlandt with the daily subcutaneous injections of certain ovarian and placental extracts on the market. The former preparation is extracted out of the ovaries of pregnant cows according to a method of Abderhalden, the latter out of placental tissue. Microscopic examinations of the ovaries after treatment showed a complete absence of large, matured follicles.

While Haberlandt is convinced of a hormonal action in securing temporary sterility in these animals, Koehler assumes a simple protein reaction. In support of his theory Haberlandt in further experiments brings evidence that temporary or permanent sterility can be brought about in the white mouse by feeding either of the above mentioned preparations daily in milk for a few months.

GROVER LIESE.

Haberlandt, L.: Hormonal Sterilization of Female Animals by Means of Insulin. Medizinische Klinik, 1927, xxiii, 1024.

Vogt recently reported that he obtained hormonal sterilization in rabbits by means of injections of insulin and because of this he considers the pancreatic hormone and the ovarian hormone as antagonists. This is incorrect. In the first place there is not one ovarian hormone but at least two, a stimulative hormone and an inhibitory one. The first one which is known as the female sex hormone can activate even the ovaries of senile animals. Vogt has failed to show that in the animals sterilized by means of insulin, maturation of follicles was inhibited, as Haberlandt accomplished by injecting ovarian preparations from pregnant cows. Furthermore, the authors who sterilized animals by injecting spermatotoxic antibodies achieved this not by means of hormonal sterilization but by humoral or immunization—sterilization. The first true hormonal sterilization experiments on female animals were performed by the writer by means of transplanting ovaries from pregnant animals into nonpregnant animals. There is no practical value in Vogt's experiments because the amount of insulin necessary to sterilize animals was too large. Furthermore Haberlandt has been able to produce in animals the same effect by the oral administration of physiologic inhibitory substances. The later offspring of animals which had been temporarily sterilized is not abnormal in any way.

J. P. GREENHILL.

Castro, Rocco: Biologic Sterilization of the Female With Injections of Seminal Fluid. Archivio di Ostetricia e Ginecologia, 1926, p. 558.

Several investigators have found that the subcutaneous injections of seminal fluid in the female produces temporary sterility of one to three months. Experiments have been carried out in the dog, rabbit and the rat. These show that a temporary sterility is produced and that if too many injections are given there is marked loss of weight representing a "protein cachexia." It is not known whether the sterility is due to a protein reaction or to a specific immunizing action.

J. W. PIERCE.

Reiprich, W.: The Incretory Influence of Male Sex Glands on Conception and Pregnancy. *Medizinische Klinik*, 1928, xxiv, 728.

The author performed a series of experiments on rabbits. He first transplanted testicles into adult females and he found that a temporary sterility resulted even in cases where the females accepted the males. He then experimented with both rabbits and white mice to see the effect of testicular implants on pregnancy and found that after transplantation all the pregnancies not only ceased to progress but the ova were absorbed. The larger the testicular transplant, the quicker was there retrogression of the gestation. This effect on pregnancy began about 8 to 10 days after the transplant was made, as proved by laparotomy. Implantation of nonspecific tissue such as muscle had no effect at all on conception and pregnancy.

The effect of the testicular transplants was not a permanent one because in some cases as soon as the transplants degenerated, conception and pregnancy took place. In three cases, laparotomy performed two months after testicular transplantation showed the uterus and ovaries greatly atrophied, but seven months later the organs were of normal size again. Some other experimenters have shown that when a male and female animal are united symbiotically, and the female is mated to another male, the female proves sterile. Others have produced sterility by injection of sperm and still others by the transplantation of ovaries of pregnant animals and also by means of placental and ovarian hormone. The question is raised whether in human beings pregnancy can be interrupted by testicular hormone.

J. P. GREENHILL.

Sippel, P.: Transplantation Material in Homoplastic Ovarian Transplantation. *Klinische Wochenschrift*, 1926, v, 269.

The most important detail in homoplastic ovarian transplantation is the careful selection of material. Sippel suggests that blood compatibility tests should be made between the donor and the recipient before any transplantation is attempted. The author uses for transplantation purposes, ovaries removed with ectopic pregnancies, early carcinomas, multiple myomas or those removed on account of some systemic disease, such as cardiac diseases, or even early cases of apical involvement of the lung. He has also used ovaries, when well developed, from patients with complete vaginal or uterine aplasia. Each ovary, before being transplanted, is sectioned and examined microscopically and only ovaries which show ripening follicles and corpora lutea and give the impression of being generally healthy are used.

The author cannot agree with Hollauer that there is any danger in using ovaries from patients who are suffering from early carcinoma or early pulmonary tuberculosis. Both these conditions, if present, can be readily identified in the ovary, both macroscopically and microscopically. The author has transplanted ovaries from 36 patients with early carcinoma without any after-effects.

The ovary to be transplanted is always kept at body temperature until used, although several times the technic of Zondek was employed, i.e., the ovary was kept on ice for from twenty-four to seventy-two hours. The author has not as yet arrived at the definite conclusion that this latter method gives as good results as the former one. It would, of course, simplify the method greatly if the results obtained by using ovaries preserved on ice for several days equalled those obtained by transplanting after a short interval during which the ovary is kept at body temperature.

The author reports a series of 127 cases of this type of ovarian transplant. The transplantation is usually done into or just under the rectus sheath. There have been no complications or after-effects other than six superficial wound infections.

RALPH A. REIS.

Lipschuetz, A.: Further Investigation on Transplantation of Artificially Preserved Ovaries. *Deutsche medizinische Wochenschrift*, 1928, liv, 701.

The author was able to demonstrate the hormonal effect of transplanted ovaries which after removal had been kept on ice for from three to sixteen days.

The experiments were carried out as homologous transplants on the guinea pig. The organ was transferred to the kidney of a castrated male and effect on the mammary glands was observed. A feminizing effect could be discovered, lasting one hundred and sixty days without decrease, obtained with an ovary kept in cold storage for three days. The ovary after a storage of sixteen days showed the same effect for at least several weeks. Microscopic examination revealed that the development of follicles was still going on in the slices of the transplanted ovary.

Cooling the ovary to 0° C. will destroy it. The temperature on ice remains between 1 and 3° C.

GRUENFELD.

Fawcett, Hadfield, and Phillips: Suprarenal Virilism. *The Bristol Medical-Chirurgical Journal*, 1926, xliii, 20.

A woman, aged seventy, was admitted to hospital for intestinal obstruction. A large tumor mass was found replacing each suprarenal gland, representing a cortical hyperplasia with diffuse fatty infiltration. The stroma was probably sarcomatous. Secondary sex characters of the patient approximated to the male type, the voice, physique, and hirsuties being masculine. Considerable hypertrophy of the clitoris was present. The uterus, ovaries, and vagina were rudimentary. No tissue resembling the male testicle was found in the pelvis.

ADAIR AND CARLSON.

Vignes, H.: The Use of Testicular Preparations in Gynecologic Ailments. *Bulletin Général de Thérapeutique*, May, 1926.

There is evidence to show that there exists a certain antagonism between the testicles and the ovaries. This evidence rests upon the following facts: (1) parabiotic experiments; (2) the condition known as free-martinism; (3) changes in sex after castration in certain animals; (4) it is difficult to graft successfully an ovary in a normal male and vice versa; (5) if an animal is first castrated, a graft of the opposite gonad will be successful.

Experimentally the injection of testicular extract or of sperm into females may occasionally cause the appearance of male characteristics or it may produce sterility.

Vignes had preparations of testicular extract made and used them for gynecologic ailments. The indications for the use of these extracts were: (1) senility, attributable to the menopause; (2) insufficient menses; (3) superabundant menses (to counterbalance the overactivity of the ovaries); (4) nervous trouble attributable to the genital function, and (5) ailments produced by continence. The results obtained by the author were not at all striking, but he intends to continue this study if the occasion again arises.

J. P. GREENHILL.

Uhlmann, Fr.: Standardization of the Ovarian Hormone. *Le Gynécologie*, 1927, xxvi, 65.

Both in the experiment and in certain clinical observations a variety of phenomena can be produced with the administration of various ovarian extracts. Naturally the question arises whether they all are due to a single active substance or whether the ovary elaborates several hormones, differing in their specific effect. The writer believes that two hormones are produced.

He employed in a large series of experiments two preparations, the one supposed to contain solely the lipoid extract of ovary, follicle and placenta, the other claimed to represent another water-soluble hormone. His main object is to find a reliable method of standardization for these two hormones which, as he endeavors to show, are clearly differentiated by their biologic effect. The lipoid extract stimulates growth of uterus, tubes, vagina, vulva and breasts; influences sexual activity as expressed in rut, and inhibits menstruation according to certain clinical reports which he seemingly accepts as conclusive. The water-soluble hormone, on the other hand, will cause hyperemia of the sexual organs, stimulate and even precipitate menstruation (according to clinical reports), and increases milk secretion.

He concludes that the lipoid extract, qualitatively and quantitatively, is best standardized on the basis of its growth effect, and only less reliably by the now generally employed Allen-Doisy method.

In contradistinction to the lipoid extract, the aqueous extract possesses characteristic pharmacologic properties. Most important among them are the effect on intestinal peristalsis and on salivary secretion. This latter effect, in his belief, represents the best and simplest method of standardization of this second water-soluble hormone.

